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11-410

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Serial Number: 08/850,353

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Phone: 308-4621

Art Unit: 1623
7A17

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_____ N.A. Sequence

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_____ Structure

_____ Bibliographic

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_____ IG

✓ STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

Everett White

08/850,353

November 16, 1998

308-4621

1623

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Please search the method of locating one or more salts of a compound of claim 1, a method of determining a useful salt of claims 2 and 3 and the composition of claims 4-15. A copy of the claims is attached hereto. A copy of the cover sheet comprising the inventor names is also attached.

White, E
08/850353

=> fil reg; d que l1; d que l2; fil caplu

FILE 'REGISTRY' ENTERED AT 11:08:35 ON 19 NOV 1998
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Stereochemical name changes have been adopted and appear in CN's beginning 6/29/98. See the online news message for details. - key terms

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON CYCLODEXTRIN/CN

L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON SALT/CN

FILE 'CAPLUS' ENTERED AT 11:08:37 ON 19 NOV 1998
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FILE COVERS 1967 - 19 Nov 1998 VOL 129 ISS 21
FILE LAST UPDATED: 19 Nov 1998 (981119/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON CYCLODEXTRIN/CN
Searcher : Shears 308-4994

L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON SALT/CN
L9 23841 SEA FILE=CAPLUS ABB=ON PLU=ON (L2 OR SALT)(5A)SOLUB?
L11 31 SEA FILE=CAPLUS ABB=ON PLU=ON L9(10A)(L1 OR CYCLODEXTRIN OR CYCLO DEXTRIN)

=> d 1-31 .bevstr

L11 ANSWER 1 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1998:203980 CAPLUS
DN 128:299432
TI The effect of water-soluble polymers on the aqueous solubility and complexing abilities of .beta.-cyclodextrin
AU Loftsson, Thorsteinn; Frioriksdottir, Hafrun
CS Pharmacology and Toxicology, Institute of Pharmacy, University of Iceland, P.O. Box 7210, Reykjavik, IS-127, Iceland
SO Int. J. Pharm. (1998), 163(1-2), 115-121
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier Science B.V.
DT Journal
LA English
AB The purpose of this study was to investigate the effects of both water-sol. polymers and various drugs on the soly. of .beta.-cyclodextrin (.beta.CD) in aq. soln. The soly. of .beta.CD in water was detd. to be 18.6 mg/mL, but the addn. of 0.25-1.00% of PVP, and heating in an autoclave (120-140.degree. for 20-40 min) increased the soly. to 21 mg/mL. The aq. soly. of .beta.CD also increased upon drug-.beta.CD complex formation. Both lipophilic and hydrophilic drugs increased the soly. of .beta.CD in water. For example, the soly. of .beta.CD in a satd. aq. soln. of carbamazepine was detd. to be 28.4 mg/mL but 53.3 mg/mL when 0.25% hydroxypropyl Me cellulose (HPMC) was present in the solns. The total soly. of .beta.CD in such aq. systems appeared to be the sum of the intrinsic soly. of .beta.CD and the soly. of the various .beta.CD complexes, i.e., the drug-.beta.CD complexes and the complexes of .beta.CD and drug-.beta.CD complexes with the water-sol. polymers. Not only did the polymer solubilize .beta.CD and its complexes, but was also able to enhance drug-.beta.CD complex formation.

L11 ANSWER 2 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1998:143356 CAPLUS
DN 128:248567
TI Method of selecting **salts** with desired **solubility** in aqueous **cyclodextrin** solution for manufacture of inclusion complexes
IN Kim, Ie Suk
PA Pfizer Inc., USA
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF

PI JP 10059871 A2 19980303 Heisei
AI JP 97-115720 19970506
PRAI US 96-60016866 19960507
DT Patent
LA Japanese
AB In selecting (pharmaceutical) **salts** having **soly.** in aq. **cyclodextrin** soln. equal to or greater than a target soly. (set by doses required for therapeutic efficacy), a series of salts are obtained, their equil. soly. in the aq. soln. is measured, then their soly. is compared with the target one. The soly. of ziprasidone tosylate, tartrate, mesylate, etc., in aq. .beta.-cyclodextrin sulfobutyl ether was measured, and the mesylate was selected as the most desirable salt.
IT **12619-70-4, Cyclodextrin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of selecting **salts** with desired **soly.** in aq. **cyclodextrin** soln. for manuf. of inclusion complexes)

L11 ANSWER 3 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:801873 CAPLUS
DN 128:66485
TI Method of selecting a salt for making an inclusion complex
IN Kim, Yesook
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
PI EP 811386 A2 19971210
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
AI EP 97-302821 19970424
PRAI US 96-16866 19960507
DT Patent
LA English
AB Claimed are a method of locating one or more salts of a compd., the **salts** having a **soly.** in a **cyclodextrin** equal to or greater than a desired target **soly.**, comprising obtaining a series of **salts** of the compd., measuring the equil. **soly.** of each **salt** in the series in the **cyclodextrin**, and comparing each measured soly. with the target soly. Ziprasidone mesylate was dissolved in a 300 mg/mL .beta.-cyclodextrin sulfobutyl ether soln. to make a concn. of 27.3 mg/mL. The soln. was sterile filtered and filled into vials to give a product to be administered orally or by injections.

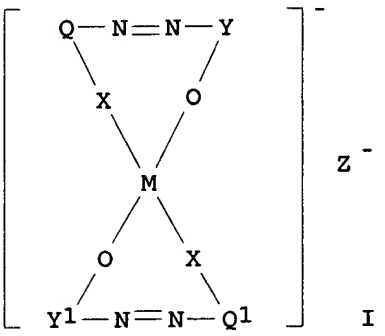
L11 ANSWER 4 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:194538 CAPLUS
DN 126:242779

TI In vitro and in vivo studies on sodium nimesulide-.beta.-cyclodextrin inclusion complex
AU Piel, G.; Delneuville, I.; Delattre, L.
CS Laboratory of Pharmaceutical Technology, Institute of Pharmacy, University of Liege, Liege, 4000, Belg.
SO Proc. Int. Symp. Cyclodextrins, 8th (1996), 487-490. Editor(s): Szejtli, J.; Szente, L. Publisher: Kluwer, Dordrecht, Neth. CODEN: 64CDAL
DT Conference
LA English
AB Nimesulide (NI), a non steroidal anti-inflammatory drug, is very poorly sol. in water. The aim of this work is to study the in vitro and in vivo characteristics of a NI Na-.beta.-cyclodextrin (CD) complex in the stoichiometric ratio 1:1. The complex was prepd. by spray-drying and the inclusion could be demonstrated by DSC and soly. method. This study has shown that the NI Na-.beta.-CD complex can increase the aq. soly. of NI (about 5000 times) as well as the soly. in acidic medium (7 times) and at pH 6.8 (34 times). A preliminary study in 3 healthy volunteers has shown promising results for further pharmaceutical development.

L11 ANSWER 5 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1997:82568 CAPLUS
DN 126:204192
TI Solubilities of the cyclodextrins in the presence of transition metal salts
AU Eddaoudi, M.; Coleman, A. W.; Junk, P. C.
CS Institut de Biologie et Chimie des Proteines, Lyon, F69367, Fr.
SO J. Inclusion Phenom. Mol. Recognit. Chem. (1996), 26(1-3), 133-151 CODEN: JIMCEN; ISSN: 0923-0750
PB Kluwer
DT Journal
LA English
AB The solubilities of .alpha.-, .beta.-, and .gamma.-cyclodextrin were measured in the presence of the 1st row transition metals: Cr3+, Mn2+, Fe3+, Co2+, Ni2+, Cu2+ and Zn2+; chlorides, nitrates and sulfates (in this case Fe2+), and, for comparison, with CaCl2, the corresponding group IIa salt. Where possible the measurements are reported as a function of the activity of the salts. In general, for the transition metals the sulfates all show a linear decrease in soly. with increasing salt activity: for the nitrates the soly. increases and then reaches a limiting value; and for the chlorides a small decrease in soly. is obsd. at low activity followed by an increase in soly. at higher salt activity. CD measurements confirm that there is no direct complexation at non-basic pH.

L11 ANSWER 6 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:609476 CAPLUS
DN 125:250612

TI Water-soluble cyclodextrin-included water-insoluble metal complex dyes
IN Murashima, Hitoshichi; Akase, Tetsumi; Kamisaka, Kazuo; Hirose, Etsuko
PA Orient Chemical Ind, Japan; Mitsubishi Electric Corp
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
PI JP 08188722 A2 19960723 Heisei
AI JP 95-18749 19950110
DT Patent
LA Japanese
OS MARPAT 125:250612
GI



I

AB Title dyes, useful for inks, etc., showing improved storage stability and light and water resistance comprise water-insol. metal complexes I [Q, Q1 = halo- and/or NO2-substituted o-aminophenol- or anthranilic acid-derived diazo residue; Y, Y1 = (amino- or NHCOR-substituted) .beta.-naphthol- or pyrazolone-derived coupler residue; M = 2- or 3-valent metal; X = O, CO2; Z = alkali metal, NH4; R = C1-4 alkyl], which are included in cyclodextrins. Thus, 4 parts C.I. Solvent Violet 21 Na salt was added to 8 parts dimethyl-.beta.-cyclodextrin in 70 parts water at 45.degree., stirred for 1 h then dried to give water-sol. dye.

L11 ANSWER 7 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:607404 CAPLUS
DN 125:250831
TI Purifying water-soluble cyclodextrin derivatives
IN Reuscher, Helmut
PA Consortium Fuer Elektrochemische Industrie Gmbh, Germany
SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
PI EP 727440 A2 19960821

DS R: BE, DE, FR, GB, IT, NL
AI EP 96-102245 19960215
PRAI DE 95-19505263 19950216
DT Patent
LA German
AB Title derivs. are purified with low material loss by reverse osmosis using .gtoreq.1 hydrophilic, asym. soln.-diffusion membrane with mol.-wt. sepn. limit 200-800.
IT **7647-14-5**, Sodium chloride, processes
RL: REM (Removal or disposal); PROC (Process)
(purifying water-**sol. cyclodextrin** derivs. by reverse osmosis using hydrophilic asym. soln.-diffusion membranes)

L11 ANSWER 8 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:469530 CAPLUS
DN 125:127882
TI Single component diazo light-tracing material
IN Niemoeller, Axel
PA Renker Gmbh und Co Kg, Germany
SO Ger., 6 pp.
CODEN: GWXXAW
PI DE 4429741 C1 19960605
AI DE 94-4429741 19940822
DT Patent
LA German
AB The title material for half dry process or thin layer process with improved quality is described. In the material comprising a flat support one or both sides coated with a light-sensitive recording material including water-**sol.** diazonium **salts**, binders, pigments, and auxiliary materials, the material contains **cyclodextrin** or **cyclodextrin** deriv. as a stabilizer.

L11 ANSWER 9 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:396063 CAPLUS
DN 125:67069
TI Treatment agents containing L-ascorbic acid and cyclodextrin for drinking water
IN Myama, Takashi; Nakamura, Masumi
PA Shizen Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
PI JP 08089934 A2 19960409 Heisei
AI JP 94-231458 19940927
DT Patent
LA Japanese
AB The treatment agents contain (a) L-ascorbic acid, (b) **cyclodextrin**, (c) glycerin-**sol. salts**,

and (d) glycerin. Optionally, the treatment agents contain EtOH and agents for modulation of clusters of H2O mols. The treatment agents may be used for prevention of discoloration of vegetables and fruits by oxidn. or for prevention of growth of microorganisms. The treatment agents provide odorless drinking water with good taste.

IT **12619-70-4, Cyclodextrin**
RL: FFD (Food or feed use); NUU (Nonbiological use, unclassified); BIOL (Biological study); USES (Uses)
(treatment agents contg. ascorbic acid, **cyclodextrin**, glycerin-**sol. salts**, and glycerin for drinking water)

L11 ANSWER 10 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:318946 CAPLUS
DN 124:346594
TI Freshness composition for reducing malodor impression on articles
IN Trinh, Toan; Cappel, Jerome Paul; Geis, Philip Anthony; Hollingshead, Judith Ann; McCarty, Mark Lee; Swartley, Donald Marion; Wahl, Errol Hoffman; Zwerdling, Susan Schmaedecke
PA Procter and Gamble Company, USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
PI WO 9604940 A1 19960222
DS W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TT, UA, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-US10210 19950810
PRAI US 94-289970 19940812
US 94-289991 19940812
US 94-289731 19940812
US 95-369845 19950106
DT Patent
LA English
AB A sprayable aq. compn. for restoring freshness to clothing and other surfaces without the need for dry cleaning/washing comprises .apprx.0.01-1% perfume, optionally, .apprx.0.1-5% water-sol. **cyclodextrin**, .apprx.0.1-10% water-**sol.** metallic **salt**, and .apprx.0-3% **solubilizing** aid. The compn. is essentially free of any material that would soil or stain fabric and contains .ltorsim.5% of low mol. wt. monohydric alcs. The compn. releases addnl. perfume fragrance upon rewetting, e.g. under conditions of perspiration. Perfumes with partitioning coeff. (Clog P values) <3, e.g. benzyl salicylate, benzyl acetate, etc. mixts., do not need alc. solvent and perfume with Clog P >3 are solubilized with solubilizing aid.

L11 ANSWER 11 OF 31 CAPLUS COPYRIGHT 1998 ACS

AN 1996:287106 CAPLUS
DN 124:325134
TI The influence of water-soluble polymers and pH on hydroxylpropyl-.beta.-cyclodextrin complexation of drugs
AU Loftsson, T.; Guomundsdottir, T. K.; Frioriksdottir, H.
CS Dep. Pharm., Univ. Iceland, Reykjavik, IS-127, Iceland
SO Drug Dev. Ind. Pharm. (1996), 22(5), 401-405
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB The effect of water-sol. polymers and ionization of the drug mols. on the cyclodextrin [mainly 2-hydroxypropyl-.beta.-cyclodextrin (HP.beta.CD)] solubilization of drugs was investigated. HP.beta.CD has significant solubilizing effect on acetazolamide, prazepam, and sulfamethoxazole in aq. solns. All 3 polymers tested, hydroxypropyl Me cellulose (HPMC), polyvinylpyrrolidone (PVP), and CM-cellulose increase the solubilizing effect of HP.beta.CD. The polymers increase the solubilization by increasing the apparent stability const. (Kc) of the drug-HP.beta.CD complex. Thus, addn. of 0.10% HPMC to the aq. complexation medium results in a 56% increase in Kc for the acetazolamide-HP.beta.CD complex and a 200% increase in Kc for the prazepam-HP.beta.CD complex. Addn. of 0.25% PVP to the complexation medium results in a 138% increase in Kc for the sulfamethoxazole-HP.beta.CD complex. The HP.beta.CD solubilization of the drugs can also be improved by ionization of the drug mol. through pH adjustments. However, larger improvements of the HP.beta.CD solubilization are obtained when both methods are used simultaneously compared to when either method is used sep.

L11 ANSWER 12 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1996:211779 CAPLUS
DN 124:242309
TI Water-soluble nimesulide salt for the treatment of inflammation
IN Pirotte, Bernard; Piel, Geraldine; Neven, Philippe; Delneuville, Isabelle; Geczy, Joszef
PA Europharmaceuticals S.A., Belg.
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
PI WO 9534533 A1 19951221
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 95-BE55 19950616
PRAI BE 94-582 19940616
DT Patent
LA French

AB A water-sol. nimesulide salt is obtained from the reaction of nimesulide with L-lysine and .beta.-cyclodextrin and formulated into various pharmaceuticals. The properties of nimesulide-L-lysine-.beta.-cyclodextrin complexes were studied. An oral liq. formulation contained the complex 5.550, hydroxypropyl cellulose 0.600, methylparaben 0.210, propylparaben 0.090, and sodium saccharin 0.100 g and water to 300 mL.

L11 ANSWER 13 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1995:823344 CAPLUS
DN 123:266127
TI Substituted cyclodextrin sulfates and their uses as growth modulating agents
IN Weisz, Paul B.; Ewing, William R.; Joullie, Madeleine M.
PA University of Pennsylvania, USA
SO U.S., 9 pp. Cont of U.S. Ser. No. 691, 168, abandoned.
CODEN: USXXAM
PI US 5441944 A 19950815
AI US 92-947417 19920918
PRAI US 89-397559 19890423
US 91-691168 19910424
DT Patent
LA English
AB The invention relates to highly water sol. substituted .alpha.-, .beta.- or .gamma.-cyclodextrin sulfates assocd. with a physiol. acceptable cation. Pathol. or otherwise undesirable cell or tissue growth and angiogenesis in mammals, is inhibited by administering a water-**sol**. substituted **cyclodextrin** sulfate **salt** (I) together with a growth-inhibiting org. compd. The growth-inhibiting compd. may be an asteroid having no inhibiting effect in the absence of I, or an org. compd. which may be an active growth inhibitor, the action of which is potentiated by I. Thus, the angiogenesis inhibitory activity of n-propoxy-.beta.-cyclodextrin sulfate was detd. by using the CAM assay.

L11 ANSWER 14 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1995:479916 CAPLUS
DN 122:309270
TI Complexation of bile acids with .beta.-cyclodextrin
AU Lee, Seung Yong; Chung, Youn Bok; Han, Kun; Choi, Song Am
CS Coll. Pharmacy, Chungbuk Natl. Univ., Chungbuk, 360-763, S. Korea
SO Yakhak Hoechi (1994), 38(1), 78-85
CODEN: YAHOA3; ISSN: 0513-4234
DT Journal
LA Korean
AB From phase **soly**. studies bile acids and bile **salts** were found to form stable inclusion complexes with .beta.-**cyclodextrin** in aq. soln. Stability const. of bile acids were larger than that of bile salts. Phase soly. diagrams of most

bile acids showed Higuchi's AL type but lithocholic acid showed BS type. Not only the soly. of bile acids but also that of .beta.-cyclodextrin increased, esp. in cases of cholic acid and ursodeoxycholic acid. Soly. increase of bile acids from their .beta.-cyclodextrin inclusion complex followed the order: cholic acid>ursodeoxycholic acid>chenodeoxycholic acid>deoxycholic acid>lithocholic acid. It seems that soly. of inclusion complexes was directly related with the hydrophilicity of bile acids.

L11 ANSWER 15 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1994:192117 CAPLUS
DN 120:192117
TI Inorganic **salt** modulation of the aqueous **solubility** of .beta.-**cyclodextrin**
AU Coleman, Anthony W.; Nicolis, Ioannis
CS Cent. Pharm., Univ. Paris-Sud, Chatenay-Malabry, 92290, Fr.
SO Supramol. Chem. (1993), 2(2-3), 93-7
CODEN: SCHEER; ISSN: 1061-0278
DT Journal
LA English
AB The effect of mono-, di- and trivalent metal **salts** on the max. aq. **soly.** of .beta.-**cyclodextrin** (.beta.-CD) has been investigated. The results show the soly. to be highly dependent on the cation charge: M+ <M2+ <M3+. For chloride as the anion, the soly. increases down Group II for a given salt concn.: Mg2+ <Ca2+ <Sr2+ <Ba2+. However for nitrate as the anion, soly. os largely cation-independent. The increased soly. allows medium-field NMR (200 MHz) to be used in the study of the .beta.-CD-thymol inclusion complex.
IT **7647-14-5**, Sodium chloride, reactions
RL: RCT (Reactant)
(aq. **soly.** of .beta.-**cyclodextrin** in presence of)

L11 ANSWER 16 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1994:31083 CAPLUS
DN 120:31083
TI Synthesis and properties of 6A-amino-6A-deoxy-.alpha.- and -.beta.-cyclodextrin
AU Brown, Susan E.; Coates, John H.; Coghlan, Daniel R.; Easton, Christopher J.; van Eyk, Stephen J.; Janowski, Wit; Lepore, Angelo; Lincoln, Stephen F.; Luo, Yin; et al.
CS Dep. Chem., Univ. Adelaide, Adelaide, 5001, Australia
SO Aust. J. Chem. (1993), 46(6), 953-8
CODEN: AJCHAS; ISSN: 0004-9425
DT Journal
LA English
AB The monotosylates obtained by treatment of .alpha.- and .beta.-cyclodextrin with p-methylbenzenesulfonyl chloride reacted

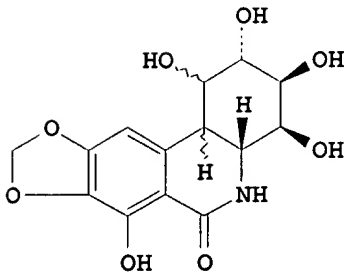
with ammonia to give the title compds. These amines are of unusually low basicity, with pKa values of 8.70 and 8.72, resp. In water at 25.degree., the hydrochloride salt of the amine derived from .beta.-cyclodextrin is approx. 40 times more sol. than .beta.-**cyclodextrin** and, through complexation, the **salt** increases the **soly**. of nabumetone over 800 times.

L11 ANSWER 17 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1992:82562 CAPLUS
DN 116:82562
TI Freeze resistance-improving agents containing water-soluble substances from of potatoes, fumarates, and/or cyclodextrin from yeasts
IN Tsubaki, Kazufumi; Suzuki, Takashi; Sugyama, Hiroshi
PA Asahi Denka Kogyo K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
PI JP 03254624 A2 19911113 Heisei
AI JP 90-50478 19900301
DT Patent
LA Japanese
AB The title agents contain water-**sol**. substances (excluding inorg. **salts**) from potatoes, fumaric acid (salts), and/or **cyclodextrin**. Dough contg. the agents show good leavening ability even after being frozen and defrosted. Dough contg. wheat flour 100, yeast 2, Na fumarate 0.2 wt. part, and other ingredients was baked into bread.

L11 ANSWER 18 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1991:687191 CAPLUS
DN 115:287191
TI Water-sol. pharmaceutical compositions containing amorphous complexes of cyclodextrin and 11-[4-[4-(4-fluorophenyl)-1-piperazinyl]butyryl]amino- 6,11-dihydrodibenzo[b,e]thiepin or its salts
IN Matsumura, Sachiko; Shirai, Hisami; Fujioka, Hiroshi; Makita, Hirokazu
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
PI JP 03072425 A2 19910327 Heisei
AI JP 90-109313 19900424
PRAI JP 89-110638 19890428
DT Patent
LA Japanese
AB Pharmaceutical compns. contain water-sol. polymers and amorphous complexes formed by cyclodextrin and the title compd. (I) or its salts. The compns. have good dispersibility in water, good stability, and good flowability. .beta.-Cyclodextrin (7.35 g) was

dissolved in 400 mL H2O at 40.degree., mixed with 1.2 g I and freeze-dried to give an amorphous complex. The complex (3.56 g) was mixed with 1.5 g hydroxypropyl methyl cellulose (II) for 3 min to give a powder compn., which released 19.5 .mu.g/mL I in H2O (pH 6.8) 15 min later, vs. <1 .mu.g/mL, for I powder.

L11 ANSWER 19 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1991:435645 CAPLUS
DN 115:35645
TI Oversaturated solutions of drug in hydroxypropyl cyclodextrins: parenteral preparation of pancratistatin
AU Torres-Labandeira, Juan J.; Davignon, Paul; Pitha, Josef
CS Health NIA, Natl. Inst., Baltimore, MD, 21224, USA
SO J. Pharm. Sci. (1991), 80(4), 384-6
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
GI



I

AB The effect of 15 cyclodextrin derivs. (polar-electroneutral, cationic, anionic, and lipophilic) and of three 2-hydroxypropyldigitonins on the soly. of pancratistatin (I), an anticancer drug, was evaluated. The direct solubilization into aq. solns. were invariably low (0.1-1.2 mg/mL compared with 50 .mu.g/mL in water). Complexes of I with hydroxypropyl .beta.-cyclodextrin were more stable (Kapp 153 M-1) than those with hydroxypropyl .gamma.-cyclodextrin (Kapp 108 M-1). Acceptable prepns. were made by dissoln. of I in a large excess (50.times.) of hydroxypropyl cyclodextrin by ammonia and then freeze drying to ammonia-free prepns. In these prepns., both the inclusion and interdispersion phenomana were operative, and the prepns. dissolved rapidly forming clear solns. of I of concns. up to 9 mg/mL. These solns. were oversatd. and while those based on hydroxypropyl .beta.-cyclodextrin pptd. within 1 h, those based on hydroxypropyl .gamma.-cyclodextrin

were stable for at least 4 h when kept in a plastic container (i.e., time sufficient for potential use in parenteral prepns.).

L11 ANSWER 20 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:538405 CAPLUS
DN 113:138405
TI High-field nuclear magnetic resonance techniques for the investigation of a .beta.-cyclodextrin:indomethacin inclusion complex
AU Djedaini, Florence; Lin, Sheng Zhao; Perly, Bruno; Wouessidjewe, Denis
CS Cent. Etud. Nucl. Saclay, Gif/Yvette, F-91191, Fr.
SO J. Pharm. Sci. (1990), 79(7), 643-6
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB The inclusion complex of indomethacin Na salt in .beta.-cyclodextrin was studied by proton NMR at high magnetic field. The continuous variation technique was used to evidence the formation of a sol. 1:1 complex in aq. soln. at physiol. pH. The effective assocn. const. was detd. by the Benesi-Hildebrand procedure to be 760 M-1 at 303 K. This technique requires NMR measurements in the presence of a very large excess of one of the complex components and, since both .beta.-**cyclodextrin** and the Na **salt** of indomethacin are sparingly **sol.** in water, NMR spectrometers operating at very high magnetic fields were used. Besides the effective assocn. const., the Benesi-Hildebrand approach allows a precise detn. of all NMR parameters of the pure inclusion complex which may be used for a complete anal. of the geometry of this complex in soln.

L11 ANSWER 21 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:210976 CAPLUS
DN 112:210976
TI Angiogenesis-inhibiting compositions comprising cyclodextrin salts
IN Folkman, Moses Judah; Weisz, Paul Burg
PA USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
PI WO 8906536 A1 19890727
DS W: AU, DK, GB, JP, KR
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE
AI WO 89-US175 19890117
PRAI US 88-145407 19880119
US 89-295638 19890110
DT Patent
LA English
AB A compn. for inhibiting undesired tissue growth, specifically angiogenesis, comprises a highly **sol.** .alpha.-, .beta.-,

or .gamma.-**cyclodextrin salt** and a latent growth-inhibiting steroid or nonsteroidal growth-inhibiting org. compd. As shown on the chorioallantoic membrane of the chick embryo, (Folkman, J. M., et al., 1983), 60 .mu.g hydrocortisone, combined with 0.05-50 .mu.g .beta.-cyclodextrin tetradecasulfate, inhibited angiogenesis. Prepn. of the cyclodextrin salts is given.

L11 ANSWER 22 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:177255 CAPLUS
DN 112:177255
TI Fish meal-contg. membrane-type food preparation
IN Muto, Masashi; Wakabayashi, Hitomi; Fukazawa, Ryutaro
PA Seiwa Oil and Chemetics Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
PI JP 01202274 A2 19890815 Heisei
AI JP 88-27121 19880208
DT Patent
LA Japanese
AB Membrane-type food is prepd. by extn. of pulverized fish meat with an actomyosin-**solubilizing salt** soln., optionally contg. **cyclodextrin** (1-50%), toprep. a gel-like material with which other components are mixed and then thin membranes are prepd. and dried at a temp. below the coagulation temp. of the proteins. Prepns. of the membrane-type food contg. cod roe, melon, yam, and Laminaria were demonstrated.

L11 ANSWER 23 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1990:38707 CAPLUS
DN 112:38707
TI Interactions of .beta.-cyclodextrin with surface active compounds: interactions of .beta.-**cyclodextrin** with surface active compounds of the ammonium **salt** type. II. **Solubilization** of pyrene in aqueous systems of .beta.-**cyclodextrin** and surface active compounds containing p-tert-butylphenoxy groups
AU Mitterhauszerova, Ludmila; Kralova, Katarina
CS Fac. Nat. Sci., Komensky Univ., Bratislava, Czech.
SO Tenside, Surfactants, Deterg. (1989), 26(5), 355-7
CODEN: TSDEES; ISSN: 0932-3414
DT Journal
LA English
AB The effect on pyrene solubilization as a result of its interaction with .beta.-cyclodextrin was studied with quaternary ammonium cation surfactants contg. 1 or 2 p-tert-butylphenoxy groups. With each surfactant, a considerable increase of pyrene solubilization as a result of .beta.-cyclodextrin complex formation was obsd. for systems contg. the surfactant in premicellar concn. The strong effect of the p-tert-butylphenoxy group on complex formation

(analogous to the micelle formation process) was noted.

L11 ANSWER 24 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1989:641317 CAPLUS
DN 111:241317
TI Complex formation of inorganic salts with .beta.-cyclodextrin
AU Buvari, Agnes; Barcza, Lajos
CS Inst. Inorg. Anal. Chem., L. Eotvos Univ., Budapest, H-1088, Hung.
SO J. Inclusion Phenom. Mol. Recognit. Chem. (1989), 7(3), 379-89
CODEN: JIMCEN
DT Journal
LA English
AB The interactions between some alkali halides, perchlorates and sulfates and .beta.-cyclodextrin were investigated by sol. spectrophotometric and preparative methods. The main conclusions were: (1) the most pronounced interaction occurred with the anions; in dil. solns. this was characterized as the formation of 1:1 complexes. In more concd. solns. ternary assocs. and more complicated ones with cations and anions were formed also. (2) Changes in the activity coeffs. or of the activity of H2O may have some role in the phenomena, but it cannot be dominant; differences due to the properties of the anions were much more pronounced than due to those of the cations or to changes of the ionic strength. (3) Real inclusion and outer sphere interactions via H bonds are also probable.

L11 ANSWER 25 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1989:483893 CAPLUS
DN 111:83893
TI Water-soluble bactericidal 2-mercaptopyridine N-oxide metal salt-cyclodextrin (derivative) inclusion compounds and cosmetics containing them
IN Nakamura, Mikihiko
PA Kao Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
PI JP 01009914 A2 19890113 Heisei
AI JP 87-164781 19870701
DT Patent
LA Japanese
AB Cosmetics, useful for controlling dandruff (no data), contain H2O-sol. bactericides prepd. by treatment of 2-mercaptopyridine N-oxide (I) salts with multivalent metals with .gtoreq.15 mol cyclodextrin or its derivs. Methylated .beta.-cyclodextrin (1 part) was mixed with 0.006 part I Zn salt in H2O at 60.degree. for 3 h to give aq. soln. contg. 0.1% I Zn salt, which was freeze-dried to give H2O-sol. I Zn salt-inclusion compd. A hair lotion was prepd. from 10 g of the above aq. soln. and 0.05 g perfume.

L11 ANSWER 26 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1989:409180 CAPLUS
DN 111:9180
TI **Solubilization** of dye **salts** in chloroform by amphiphilic .beta.-**cyclodextrin** derivatives
AU Takahashi, Hisao; Irinatsu, Yuichi; Tamura, Shoji; Tagaki, Waichiro
CS Fac. Eng., Osaka City Univ., Osaka, 558, Japan
SO Yukagaku (1989), 38(1), 65-71
CODEN: YKGKAM; ISSN: 0513-398X
DT Journal
LA English
AB Two dye salts, Me orange (I) and ammonium 8-anilino-1-naphthalenesulfonate (II), were efficiently solubilized in CHCl3 in the presence of some CHCl3-sol. lipophilic .beta.-cyclodextrin (III) derivs. (LCD). The solubilization was tested as the extn. of I and II from water to CHCl3 or as the dissoln. of solid I. In the LCD 7 primary hydroxyl groups of III were replaced with either dodecylthio, dodecylsulfinyl, or dodecylamino groups, with 14 secondary hydroxyl groups being left free. Host-guest complexation in CHCl3 appeared to be important for the solubilization.

L11 ANSWER 27 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1988:77531 CAPLUS
DN 108:77531
TI Process for manufacture of water-**soluble** **cyclodextrin** polymers with low **salt** content
IN Szejtli, Jozsef; Hoklits, Istvan; Keszler, Balazs; Kovacs, Gabor; Fenyvesi, Eva
PA Chinoin Gyogyszer es Vegyeszeti Termekek Gyara Rt., Hung.
SO Hung. Teljes, 10 pp.
CODEN: HUXXBU
PI HU 41824 A2 19870528
AI HU 85-2839 19850726
DT Patent
LA Hungarian
AB The condensation of cyclodextrins and epoxy compds. is accomplished in the presence of an insol. basic polyelectrolyte which is added to an aq.-alk. reaction medium in an amt. of 10-600% based on the cyclodextrin wt. The cyclodextrin-contg. soln. is sepd. from the polyelectrolyte and passed through a desalination column contg. an OH-form anion exchanger. ClCH2CO2H (28.4 g) and then 170 g .beta.-cyclodextrin was added to a stirred soln. of 12 g NaOH in 108 mL H2O and stirred for 40 min at room temp. Sep., 12 g NaOH are dissolved in 36 cm3 H2O and this soln. was added drop-wise at 1 mL/min to the cyclodextrin-contg. flask and heated to 60.degree. for 60 min. Sep., 900 mL Varion AD resin mixed with 250 mL H2O was heated to 60.degree. and added to the flask contg. the cyclodextrin soln. At const. temp., 138.7 g epichlorohydrin was added over 1.5 h, then the soln. was mixed at 60.degree. for 10 h. The reaction

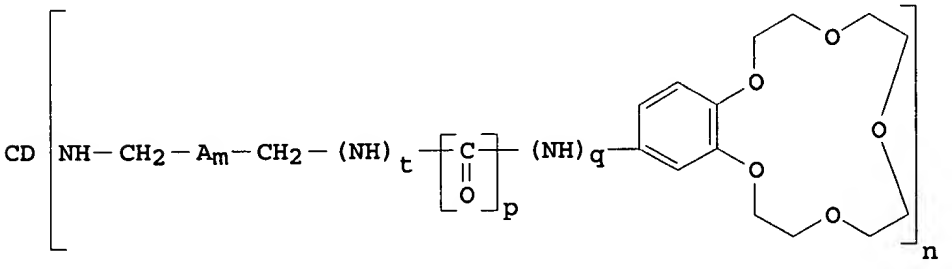
was brought to completion by cooling and the resin filtered out. The filtrate was mildly basic, had 251 g solids, and NaCl content 1%. The filtrate was further purified in the column contg. Varion KS-H and Varion AD-OH ion exchanger, producing a product which was practically salt-free.

L11 ANSWER 28 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1987:446073 CAPLUS
DN 107:46073
TI Solubilization of cyclodextrin inclusion compounds
IN Sato, Mitsukatsu; Yagi, Yoshiaki; Nishimura, Masami; Ishikura, Tomoyuki
PA Sanraku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
PI JP 62072628 A2 19870403 Showa
AI JP 85-212198 19850927
DT Patent
LA Japanese
AB Sparingly sol. cyclodextrin inclusion compds. are made sol. by mixing with C6-18 satd. or unsatd. fatty acid Na salt, Na lauryl sulfate, Na cholic acid, or Na benzoate. Thus, 16 g .beta.-cyclodextrin was added to 30 mL H2O and mixed with 4 g of a perfume oil. The mixt. was stirred vigorously for 60 min and freeze-dried. A bath prepn. was prepd. contg. the inclusion compd. 5, Na2SO4 80, NaCl 13, and Na benzoate 2 parts by wt. This prepn. was added at 1% (wt./vol.) to warm water, and rapid dissoln. was obsd.

L11 ANSWER 29 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1986:191926 CAPLUS
DN 104:191926
TI Mixing agent for hydraulic cement
IN Sasaki, Isamu; Kamisaki, Yoshiaki; Matsui, Fumio; Kamoi, Noritoshi
PA Showa Denko K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
PI JP 61021944 A2 19860130 Showa
AI JP 84-140678 19840709
DT Patent
LA Japanese
AB The title material contains 50-95 wt.% water-**sol**. sulfonate **salt**-melamine resin and 5-50 wt.% **cyclodextrin**. The flowability of the concrete mixt. does not decrease in 90 min. Thus, 90 wt.% Melment L-10 and 10 wt.% of .gamma.-cyclodextrin were mixed to obtain an agent. The concrete slurry of water-cement ratio 54.5%, sand-aggregate ratio 48%, and cement 320 kg/m3 contg. the mixing agent 0.4% showed slump index 17.5 cm after 90 min and 28-day compressive strength 451 kg/cm2.

L11 ANSWER 30 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1986:168704 CAPLUS
DN 104:168704
TI Effect of **cyclodextrins** on sparingly **soluble salts**
AU Hirsch, Warren; Fried, Vojtech; Altman, Lawrence
CS Brooklyn Coll., City Univ. New York, Brooklyn, NY, 11210, USA
SO J. Pharm. Sci. (1985), 74(10), 1123-5
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB On addn. of various **cyclodextrins**, the increase in **soly**. of some **salts** of biol. interest has been monitored using electrochem. concn. cells. A math. model has been developed to calc. the equil. consts. for the formation of inclusion complexes composed of the large, org. anions inside the cyclodextrin cavities. One stability const. detd. by this method has been verified by visible spectrophotometry.

L11 ANSWER 31 OF 31 CAPLUS COPYRIGHT 1998 ACS
AN 1985:46225 CAPLUS
DN 102:46225
TI Complexing cyclodextrin crown ethers
IN Toke, Laszlo; Agai, Bela; Bitter, Istvan; Szejtli, Jozsef
PA Chinoin Gyogyszer es Vegyeszeti Termekek Gyara Rt., Hung.
SO Hung. Teljes, 24 pp.
CODEN: HUXXBU
PI HU 29101 O 19840130
AI HU 81-2733 19810922
DT Patent
LA Hungarian
GI



I

AB The crown ether part of a cyclodextrin-crown ether mol. I (CD = .beta.-cyclodextrinyl; A = CH2OCH2; m = 0-2; n = 1, 2; p, q, t = 0,

1) complexes with the metal ions, esp. alkali or alk. earth metals, while the apolar anionic part is complexed by the **cyclodextrin** part of I, thus providing good water **soly**. and stability to the **salt** like org. compds. (e.g., dyes, photostabilizers). The prepn. of these complexes and their precursors are described along with the uptake of Na 2,4-dinitrophenolate through a stomach wall model membrane using the cyclodextrin-crown ether complex I (CD = .beta.-cyclodextrinyl; A = CH2OCH2; m = 2; n = 1; t = p = q = 1), where the crown ether part complexed with Na and the cyclodextrin took in the dinitrophenolate anion for complete mol. packaging.

=> d his l12; d 1-30 bib abs

(FILE 'CAPLUS' ENTERED AT 11:02:08 ON 19 NOV 1998)

FILE 'REGISTRY' ENTERED AT 11:08:35 ON 19 NOV 1998

FILE 'CAPLUS' ENTERED AT 11:08:37 ON 19 NOV 1998

FILE 'USPATFULL' ENTERED AT 11:09:11 ON 19 NOV 1998
L12 30 S L11

L12 ANSWER 1 OF 30 USPATFULL
AN 1998:108399 USPATFULL
TI Pharmaceutical formulation
IN Rubinfeld, Joseph, Danville, CA, United States
PA Supergen, Inc., San Ramon, CA, United States (U.S. corporation)
PI US 5804568 980908
AI US 97-790223 970203 (8)
RLI Continuation of Ser. No. US 94-297249, filed on 26 Aug 1994, now patented, Pat. No. US 5602112 which is a continuation-in-part of Ser. No. US 93-116724, filed on 3 Sep 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-900664, filed on 19 Jun 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Wilson Sonsini Goodrich & Rosati
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1519
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions of matter comprising a substituted cyclodextrin and cytotoxic compound, especially cytotoxic drugs such as antibiotic, anti-fungal and anti-neoplastic, drugs are claimed. The

compositions cause significantly less ulceration compared to the same formulation of cytotoxic compound without cyclodextrin compound when extravasated. The compositions may also cause less vascular irritation compared to the same formulation of cytotoxic compound without cyclodextrin when administered intravenously without extravasation. Compositions of matter comprising watersoluble cytotoxic agents, especially anticancer drugs and anti-ulceration effective or anti-irritatioin effective amounts of cyclodextrin compounds are also claimed. Methods for reducing the likelihood of ulceration and or irritation when administering the compositions according to the invention are also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 2 OF 30 USPATFULL
AN 1998:95542 USPATFULL
TI Guanidino protease inhibitors
IN Lu, Tianbao, Exton, PA, United States
Illig, Carl R., Phoenixville, PA, United States
Tomczuk, Bruce E., Collegeville, PA, United States
Soll, Richard M., Lawrenceville, NJ, United States
Subasinghe, Nalin L., West Chester, PA, United States
Bone, Roger F., Bridgewater, NJ, United States
PA 3-Dimensional Pharmaceuticals, Inc., Exton, PA, United States (U.S. corporation)
PI US 5792769 980811
AI US 96-698401 960815 (8)
RLI Continuation-in-part of Ser. No. US 95-536939, filed on 29 Sep 1995, now abandoned
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond
LREP Sterne, Kessler Goldstein & Fox P.L.L.C.
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4363
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula: ##STR1## wherein R.sup.1 --R.sup.4, R.sup.7 --R.sup.8, R.sup.a, R.sup.b, R.sup.c, Y, Z, n and m are set forth in the specification, as well as hydrates, solvates or pharmaceutically acceptable salts thereof, that inhibit a number of proteolytic enzymes are described. Also described are methods for preparing the compounds of Formula I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 3 OF 30 USPATFULL

AN 1998:85919 USPATFULL
TI Composition for reducing malodor impression on inanimate surfaces
IN Trinh, Toan, Maineville, OH, United States
Cappel, Jerome Paul, Cincinnati, OH, United States
Geis, Philip Anthony, West Chester, OH, United States
Hollingshead, Judith Ann, Batavia, OH, United States
McCarty, Mark Lee, Loveland, OH, United States
Zwerdling, Susan Schmaedecke, Wyoming, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5783544 980721
AI US 97-834611 970414 (8)
RLI Division of Ser. No. US 95-543350, filed on 16 Oct 1995, now patented, Pat. No. US 5663134 which is a continuation of Ser. No. US 94-289991, filed on 12 Aug 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Green, Anthony
LREP Aylor, Robert B.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1432
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an aqueous composition for reducing malodor impression. The composition comprises from about 0.01% to about 1%, by weight of the composition, of perfume wherein the perfume preferably comprises ingredients having a Clog P of 3 or smaller. Optionally, but preferably, the composition comprises from about 0.1% to about 5%, by weight of the composition of, water-soluble cyclodextrin, from about 0.1% to about 10%, by weight of the composition, of water-soluble metallic salt, from about 0% to about 3%, by weight of the composition, of solubilizing aid. The composition is essentially free of any material that would soil or stain fabric and contains less than about 5%, by weight of the composition of low molecular weight monohydric alcohols.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 4 OF 30 USPATFULL
AN 1998:79153 USPATFULL
TI Lipophilic oligosaccharide antibiotic compositions
IN Patel, Mahesh G., Verona, NJ, United States
Gullo, Vincent P., Liberty Corner, NJ, United States
Hare, Roberta S., Gillette, NJ, United States
Loebenberg, David, Monsey, NY, United States
Kwon, Heewon Y., Warren, NJ, United States
Miller, George H., Montville, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S.

corporation)
PI US 5776912 980707
AI US 96-770470 961220 (8)
DT Utility
EXNAM Primary Examiner: Peselev, Elli
LREP Hoffman, Thomas D.
CLMN Number of Claims: 27
ECL Exemplary Claim: 20,27
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1179
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An aqueous pharmaceutical composition comprising a lipophilic oligosaccharide antibiotic salt, e.g., the N-methylglucamine salt of the everninomicin-type antibiotic of Formula III together with a binding agent such as human serum albumin or recombinant human albumin and a tonicity agent such as mannitol, is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 5 OF 30 USPATFULL
AN 1998:57970 USPATFULL
TI Water-soluble nimesulide salt and its preparation, aqueous dolution containing it, nimesulide-based combinations and their uses
IN Pirotte, Bernard, rue Tollet 5, 4680 Oupeye, Belgium
Piel, Geraldine, Quai de la Boverie 41, 4020 Liege, Belgium
Neven, Philippe, rue Neuve 11, 4460 Grace-Hollogne, Belgium
Delneuville, Isabelle, rue Henri Delvaux 34, 4430 Ans, Belgium
Geczy, Joszef, avenue de Wolvendael 21, Boite 6, 1180 Brussels, Belgium
PI US 5756546 980526
WO 9534533 951221
AI US 96-596348 960611 (8)
WO 95-BE55 950616
960611 PCT 371 date
960611 PCT 102(e) date
PRAI BE 94-582 940616
DT Utility
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: Padmanabhan, Sreeni
LREP Birch, Stewart, Kolasch & Birch, LLP
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 28 Drawing Page(s)
LN.CNT 698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Water-soluble nimesulide salt consisting of the product of reaction of nimesulide and of L-lysine and its preparation, aqueous solution containing it, nimesulide-based combinations with

cyclodextrins and their uses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 6 OF 30 USPATFULL
AN 1998:14875 USPATFULL
TI Adjunctive polymer system for use with medical device
IN Dunn, Richard L., Fort Collins, CO, United States
Yewey, Gerald L., Fort Collins, CO, United States
Southard, Jeffrey L., Fort Collins, CO, United States
Urheim, John E., Fort Collins, CO, United States
PA Atrix Laboratories, Inc., Fort Collins, CO, United States (U.S. corporation)
PI US 5717030 980210
AI US 96-761522 961206 (8)
RLI Continuation of Ser. No. US 95-475097, filed on 7 Jun 1995 which is a division of Ser. No. US 94-226006, filed on 8 Apr 1994
DT Utility
EXNAM Primary Examiner: Merriam, Andrew E. C.
LREP Merchant, Gould, Smith, Edell, Welter & Schmidt
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1012
AB A medical device which is a surgically implantable device coated with an adjunctive polymer system. The adjunctive polymer system forms a solid matrix when introduced into a human or animal body. The adjunctive polymer system can contain a drug or a medicament which is released over time from the solid matrix. The adjunctive polymer system contacts body tissue into which the surgically implantable device is implanted.

L12 ANSWER 7 OF 30 USPATFULL
AN 1998:9487 USPATFULL
TI Estramustine formulations with improved pharmaceutical properties
IN Martini, Alessandro, Milan, Italy
Maccari, Giuseppe, Voghera, Italy
Muggetti, Lorena, Milan, Italy
Colombo, Giuseppe, Milan, Italy
Buzzi, Giovanni, Milan, Italy
PA Pharmacia AB, Stockholm, Sweden (non-U.S. corporation)
PI US 5712260 980127
WO 9609072 960328
AI US 96-635956 960506 (8)
WO 95-EP3438 950901
960506 PCT 371 date
960506 PCT 102(e) date
PRAI GB 94-19153 940922

DT Utility
EXNAM Primary Examiner: Kight, John; Assistant Examiner: Lee, Howard C.
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 445
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a pharmaceutical composition comprising an estramustine derivative and a cyclodextrin, particularly in the manufacture of a medicament suitable for the oral administration of an estramustine derivative to a patient suffering from a tumor.

Estramustine derivatives according to the invention are, for example, compounds of general formula (I) ##STR1## wherein R is ##STR2## in which R.sub.1 is C.sub.1 -C.sub.4 alkyl and n is 0, 1 or 2, and the pharmaceutically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 8 OF 30 USPATFULL
AN 1998:4251 USPATFULL
TI Adjunctive polymer system for use with medical device
IN Dunn, Richard L., Fort Collins, CO, United States
Yewey, Gerald L., Fort Collins, CO, United States
Southard, Jeffrey L., Fort Collins, CO, United States
Urheim, John E., Fort Collins, CO, United States
PA Atrix Laboratories, Inc., Fort Collins, CO, United States (U.S. corporation)
PI US 5707647 980113
AI US 96-749029 961114 (8)
RLI Continuation of Ser. No. US 95-487545, filed on 7 Jun 1995, now abandoned which is a division of Ser. No. US 94-226006, filed on 4 Apr 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Merriam, Andrew E. C.
LREP Merchant, Gould, Smith, Edell, Welter & Schmidt
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1035
AB A medical device which is a surgically implantable device coated with an adjunctive polymer system. The adjunctive polymer system forms a solid matrix when introduced into a human or animal body. The adjunctive polymer system can contain a drug or a medicament which is released over time from the solid matrix. The adjunctive polymer system contacts body tissue into which the surgically implantable device is implanted.

L12 ANSWER 9 OF 30 USPATFULL
AN 97:99279 USPATFULL
TI Selective alkylations of cyclodextrins leading to derivatives which have a rigidly extended cavity
IN Pitha, Josef, 417 S. Anglesea St., Baltimore, MD, United States 21224
PI US 5681828 971028
AI US 95-575075 951219 (8)
DT Utility
EXNAM Primary Examiner: Kight, John; Assistant Examiner: White, Everett
LREP Hendricks, Glenna; Gates, Stephen
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1036
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB By controlling basicity of the reaction, it is possible to alkylate preferentially the secondary hydroxyls of cyclodextrins. These hydroxyls surround the principal, wide, entry into the cyclodextrin cavity and, thus, their substitution by suitably chosen substituents can improve the formation of inclusion complexes. By methods of the invention, cyclodextrin derivatives substituted with fused 1,4-dioxane ring(s) can be obtained. If a reagent with one alkylating moiety is used, a mixture of ethers of cyclodextrin is formed. Using methods of this invention, up to 96% of the substitution can be directed to the secondary hydroxyls.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 10 OF 30 USPATFULL
AN 97:96856 USPATFULL
TI Pharmaceutical composition comprising diclofenac and cyclodextrin
IN Bodley, Mark David, Charlo, South Africa
Glintenkamp, Lueta Ann, The Barn, South Africa
Penkler, Lawrence John, Lorraine, South Africa
van Oudtshoorn, Michiel Coenraad Bosch, Monument Park, South Africa
PA Farmarc Nederland BV, Amsterdam, Netherlands (non-U.S. corporation)
PI US 5679660 971021
AI US 94-352866 941202 (8)
PRAI ZA 93-9031 931202
DT Utility
EXNAM Primary Examiner: Fonda, Kathleen K.
LREP Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 13

ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 617
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of preparing an injectable pharmaceutical or veterinary composition which comprises either diclofenac or a salt thereof and 2-hydroxypropyl beta-cyclodextrin, or an inclusion complex of diclofenac or a salt thereof and 2-hydroxypropyl beta-cyclodextrin, includes the step of dissolving either the diclofenac or salt thereof and the 2-hydroxypropyl beta-cyclodextrin, or the inclusion complex, in water to form a solution, the water having been acidified to a pH such that the pH of the solution is from 6.0 to 8.5 inclusive, in the absence of a phosphate buffer. The composition so produced has good stability on storage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 11 OF 30 USPATFULL
AN 97:91512 USPATFULL
TI Inclusion complex of beta-cyclodextrin and diclofenac, its preparation and use
IN Bodley, Mark David, Port Elizabeth, South Africa
Caira, Mino Rodolfo, Cape Town, South Africa
Glintenkamp, Lueta Ann, Port Elizabeth, South Africa
Griffith, Vivienne Jean, Cape Town, South Africa
Nassimbeni, Luigi Renzo, Cape Town, South Africa
Nicholson, Douglas George Murray, Port Elizabeth, South Africa
Penkler, Lawrence John, Port Elizabeth, South Africa
Van Oudtshoorn, Michiel Coenraad Bosch, Pretoria, South Africa
PA Farmarc Nederland BV, Amsterdam, Netherlands (non-U.S. corporation)
PI US 5674854 971007
AI US 94-319548 941007 (8)
PRAI ZA 93-7480 931008
DT Utility
EXNAM Primary Examiner: Kight, John; Assistant Examiner: Lee, Howard C.
LREP Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 729
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An inclusion complex of diclofenac, preferably as diclofenac sodium, and an unsubstituted beta-cyclodextrin has the formula 1 molecule of diclofenac to 1 molecule of the unsubstituted beta-cyclodextrin and preferably from 5 to 11 water molecules. The inclusion complex may be formulated as a pharmaceutical

composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 12 OF 30 USPATFULL
AN 97:86583 USPATFULL
TI Composition for reducing malodor impression of inanimate surfaces
IN Trinh, Toan, Maineville, OH, United States
Cappel, Jerome Paul, Cincinnati, OH, United States
Geis, Philip Anthony, West Chester, OH, United States
Hollingshead, Judith Ann, Batavia, OH, United States
McCarty, Mark Lee, Loveland, OH, United States
Zwerdling, Susan Schmaedecke, Wyoming, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5670475 970923
AI US 96-617949 960313 (8)
RLI Continuation of Ser. No. US 94-289731, filed on 12 Aug 1994
DT Utility
EXNAM Primary Examiner: Caldarola, Glenn A.; Assistant Examiner: Ghyka, Alexander G.
LREP Aylor, Robert B.
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1348
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an aqueous composition for reducing malodor impression. The composition comprises from about 0.01% to about 1%, by weight of the composition, of perfume wherein the perfume preferably comprises ingredients having a Clog P of 3 or smaller. Optionally, but preferably, the composition comprises from about 0.1% to about 5%, by weight of the composition of, water-soluble cyclodextrin, from about 0.1% to about 10%, by weight of the composition, of water-soluble metallic salt, from about 0% to about 3%, by weight of the composition, of solubilizing aid. The composition is essentially free of any material that would soil or stain fabric and contains less than about 5%, by weight of the composition of low molecular weight monohydric alcohols.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 13 OF 30 USPATFULL
AN 97:78405 USPATFULL
TI Composition for reducing malodor impression on inanimate surfaces
IN Trinh, Toan, Maineville, OH, United States
Cappel, Jerome Paul, Cincinnati, OH, United States
Geis, Philip Anthony, West Chester, OH, United States

Hollingshead, Judith Ann, Batavia, OH, United States
McCarty, Mark Lee, Loveland, OH, United States
Zwerdling, Susan Schmaedecke, Wyoming, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5663134 970902
AI US 95-543350 951016 (8)
RLI Continuation of Ser. No. US 94-289991, filed on 12 Aug 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Wood, Elizabeth D.; Assistant Examiner: Ghyka, Alexander G.
LREP Aylor, Robert B.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1302
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an aqueous composition for reducing malodor impression. The composition comprises from about 0.01% to about 1%, by weight of the composition, of perfume wherein the perfume preferably comprises ingredients having a Clog P of 3 or smaller. Optionally, but preferably, the composition comprises from about 0.1% to about 5%, by weight of the composition of, water-soluble cyclodextrin, from about 0.1% to about 10%, by weight of the composition, of water-soluble metallic salt, from about 0% to about 3%, by weight of the composition, of solubilizing aid. The composition is essentially free of any material that would soil or stain fabric and contains less than about 5%, by weight of the composition of low molecular weight monohydric alcohols.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 14 OF 30 USPATFULL
AN 97:59194 USPATFULL
TI Methods of inhibiting angiogenesis and tumor growth, and treating ophthalmologic conditions with angiostatic and therapeutic steroids
IN Petrow, Vladimir, Chapel Hill, NC, United States
Proia, Alan D., Durham, NC, United States
PA Duke University, Durham, NC, United States (U.S. corporation)
PI US 5646136 970708
AI US 94-177287 940104 (8)
DT Utility
EXNAM Primary Examiner: Burn, Brian M.
LREP Bell, Seltzer, Park & Gibson
CLMN Number of Claims: 13
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 2399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating angiogenesis, tumors, and ocular hypertension with steroids are disclosed herein. The steroids have angiostatic activity with reduced glucocorticoid activity.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 15 OF 30 USPATFULL
AN 97:49625 USPATFULL
TI Methods of inhibiting restenosis
IN Herrmann, Howard C., Yardley, PA, United States
Barnathan, Elliot, Havertown, PA, United States
Weisz, Paul, Yardley, PA, United States
PA The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PI US 5637575 970610
AI US 93-81493 930623 (8)
DCD 20080528
RLI Continuation of Ser. No. US 91-790320, filed on 12 Nov 1991, now abandoned which is a continuation-in-part of Ser. No. US 91-691168, filed on 24 Apr 1991, now abandoned which is a continuation of Ser. No. US 89-397559, filed on 23 Aug 1989, now abandoned which is a continuation-in-part of Ser. No. US 89-434659, filed on 9 Nov 1989, now patented, Pat. No. US 5019562 which is a continuation of Ser. No. US 89-295638, filed on 10 Jan 1989, now abandoned which is a continuation-in-part of Ser. No. US 88-145407, filed on 19 Jan 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Duane, Morris & Heckscher
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 602
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are compositions and methods effective for inhibiting restenosis. In particular, the present invention provides compositions for inhibiting undesired smooth muscle cell growth or proliferation following angioplasty in mammals, said composition comprising active agents comprising a very water-soluble derivative of cyclodextrin. The invention also provides methods of inhibiting undesired smooth muscle cell growth or proliferation following angioplasty in mammals comprising orally administering to the mammal a growth-inhibiting amount of an active agent comprising a very water-soluble derivative of cyclodextrin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 16 OF 30 USPATFULL
AN 97:36200 USPATFULL
TI Aqueous solution inclusion complexes of benzothiophene compounds with water soluble cyclodextrins, and pharmaceutical formulations and methods thereof
IN Bryant, Henry U., Indianapolis, IN, United States
Cullinan, George J., Trafalgar, IN, United States
Francis, Paul C., Indianapolis, IN, United States
Magee, David E., Indianapolis, IN, United States
Sweetana, Stephanie A., Bloomington, IN, United States
Thakkar, Arvind L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5624940 970429
AI US 95-497327 950630 (8)
RLI Continuation of Ser. No. US 93-166788, filed on 14 Dec 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Clardy, S. Mark
LREP Strode, Janelle D.; Boone, David E.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides aqueous inclusion complexes of certain known benzothiophene compounds, particularly Raloxifene, and water soluble cyclodextrins. Also provided are pharmaceutical compositions of such inclusion complexes, and methods of using these complexes for inhibiting bone loss and reducing serum cholesterol in mammals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 17 OF 30 USPATFULL
AN 97:36174 USPATFULL
TI Lipophilic oligosaccharide antibiotic salt compositions
IN Patel, Mahesh, Verona, NJ, United States
Gullo, Vincent P., Liberty Corner, NJ, United States
Hare, Roberta, Gilette, NJ, United States
Loebenberg, David, Monsey, NY, United States
Morton, James B., Belleville, NJ, United States
Miller, George H., Montville, NJ, United States
Kwon, Heewon Y., Edison, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 5624914 970429
AI US 94-211700 940412 (8)

WO 92-US8565 921014
940412 PCT 371 date
940412 PCT 102(e) date
DT Utility
EXNAM Primary Examiner: Kight, John; Assistant Examiner: White, Everett
LREP Hoffman, Thomas D.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1351
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pharmaceutically acceptable compositions of matter comprising a lipophilic oligosaccharide antibiotic, e.g., the everninomicin-type antibiotic of Formula III, at least a stoichiometric amount of a base, e.g., N-methylglucamine, an amount of, e.g., hydroxypropyl-.beta.-cyclodextrin, and optionally a pharmaceutically acceptable non-ionic surfactant, e.g., Tween-80, pharmaceutical compositions containing such compositions of matter, methods of treating and preventing susceptible bacterial infections in animals especially human beings as well as a method of preventing adverse reaction syndrome while simultaneously delivering an antiinfective amount of a lipophilic oligosaccharide antibiotic such as that of Formula III to said animals as well as the use of the compositions of matter for the preparation of a medicament for such treating or preventing are disclosed. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 18 OF 30 USPATFULL
AN 97:20272 USPATFULL
TI Calcium-enriched drink and method for producing the same
IN Kaji, Nobuo, Tokyo, Japan
Mizusawa, Susumu, Tokyo, Japan
Sahashi, Masayuki, Tokyo, Japan
Tsuchida, Takako, Tokyo, Japan
PA Kabushiki Kaisha Yakult Honsha, Tokyo, Japan (non-U.S. corporation)
PI US 5609898 970311
AI US 95-567240 951205 (8)
PRAI JP 94-330348 941207
DT Utility
EXNAM Primary Examiner: Pratt, Helen
LREP Sughrue, Mion, Zinn, Macpeak & Seas
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 486
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a soybean milk or milk drink which is highly enriched with calcium and which has excellent taste and storage stability. The soybean milk or milk drink is enriched with calcium by adding a hardly soluble calcium compound thereto, and by adding colloidal microcrystalline cellulose and low-strength agar in such amounts as not to exceed a viscosity of 40 cp, to thereby stabilize the calcium in the soybean milk or milk drink.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 19 OF 30 USPATFULL
AN 97:12451 USPATFULL
TI Pharmaceutical formulation
IN Rubinfeld, Joseph, Danville, CA, United States
PA SuperGen, Inc., Emeryville, CA, United States (U.S. corporation)
PI US 5602112 970211
AI US 94-297249 940826 (8)
RLI Continuation-in-part of Ser. No. US 93-116724, filed on 3 Sep 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-900664, filed on 19 Jun 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Fineman, Elliott L.
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1542
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions of matter comprising a substituted cyclodextrin and cytotoxic compound, especially cytotoxic drugs such as antibiotic, anti-fungal and anti-neoplastic, drugs are claimed. The compositions cause significantly less ulceration compared to the same formulation of cytotoxic compound without cyclodextrin compound when extravasated. The compositions may also cause less vascular irritation compared to the same formulation of cytotoxic compound without cyclodextrin when administered intravenously without extravasation. Compositions of matter comprising watersoluble cytotoxic agents, especially anti-cancer drugs and anti-ulceration effective or anti-irritation effective amounts of cyclodextrin compounds are also claimed. Methods for reducing the likelihood of ulceration and or irritation when administering the compositions according to the invention are also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 20 OF 30 USPATFULL
AN 96:108932 USPATFULL
TI Composition for reducing malodor impression on inanimate surfaces

IN Trinh, Toan, Maineville, OH, United States
Cappel, Jerome P., Cincinnati, OH, United States
Geis, Philip A., West Chester, OH, United States
McCarty, Mark L., Loveland, OH, United States
Zwerdling, Susan S., Wyoming, OH, United States
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 5578563 961126
AI US 94-289733 940812 (8)
DT Utility
EXNAM Primary Examiner: Lieberman, Paul; Assistant Examiner: Dusheck, Caroline L.
LREP Aylor, Robert B.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1617
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an aqueous composition for reducing malodor impression. The composition comprises from about 0.1% to about 20%, by weight of the composition, of solubilized, water-soluble alkali metal salt selected from the group consisting of carbonate salts, bicarbonate salts, and mixtures thereof, from about 0.01% to about 1%, by weight of the composition, of perfume. Optionally, but preferably, the composition comprises from about 0% to about 5%, by weight of the composition, of solubilized, water-soluble cyclodextrin, and from about 0% to about 3%, by weight of the composition, of solubilizing aid. The composition is essentially free of any material that would soil or stain fabric and contains less than about 5%, by weight of the composition, of low molecular weight monohydric alcohol, and has a pH of from about 7.5 to about 10.5.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 21 OF 30 USPATFULL
AN 96:63015 USPATFULL
TI Method of producing highly water-soluble cyclodextrin complex
IN Ohmachi, Yoshihiro, Tsukuba, Japan
Tsugawa, Yoshihiko, Kashiwara, Japan
Nagai, Akihiro, Toyono-gun, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5536623 960716
AI US 93-11457 930129 (8)
PRAI JP 92-15236 920130
JP 92-332021 921211
DT Utility
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: Scalzo,

Catherine Kilby
LREP Conlin, David G.; Corless, Peter F.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 800
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides 1) a method of producing a complex of a fumagillol derivative of the formula: ##STR1## wherein R.sup.1 is hydrogen; R.sup.2 is halogen, N(O)mR.sup.5 R.sup.6, N+R.sup.5 R.sup.6 R.sup.7.X-- or S(O)nR.sup.5, wherein R.sup.5, R.sup.6 and R.sup.7 are independently an optionally substituted hydrocarbon group or an optionally substituted heterocyclic group; X-- is a counter anion; m is 0 or 1; n is an integer of 0 to 2; and R.sup.5 and R.sup.6 together with the adjacent nitrogen or sulfur atom may form an optionally substituted nitrogen- or sulfur-containing heterocyclic group which may form a condensed ring; or R.sup.1 and R.sup.2 are combined to represent a chemical bond; R.sup.3 is 2-methyl-1-propenyl group or isobutyl group; A is oxygen or NR.sup.8, wherein R.sup.8 is hydrogen or an optionally substituted lower alkyl or aryl group; and R.sup.4 is hydrogen, an optionally substituted hydrocarbon group or an optionally substituted acyl group; or a physiologically acceptable **salt** thereof, with a highly water-**soluble** **cyclodextrin** derivative, which comprises mixing the fumagillol derivative or a physiologically acceptable **salt** thereof with the highly water-**soluble** **cyclodextrin** derivative into an aqueous solution, the concentration of the highly water-soluble cyclodextrin derivative being at about 100 mg/ml or more, and 2) the complex of the fumaggillol derivative (I) or physiologically acceptable **salt** thereof with the highly water-**soluble** **cyclodextrin** derivative obtained by the production method 1).

The complex of the fumagillol derivative (I) or physiologically acceptable **salt** thereof with the highly water-**soluble** **cyclodextrin** derivative is highly soluble in water, highly stable in storage and can be used as a preparation for injection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 22 OF 30 USPATFULL
AN 96:3723 USPATFULL
TI Composition of stabilized fibroblast growth factor
IN Fukunaga, Kazuhiro, Tokyo, Japan
Hijikata, Shigeki, Tokyo, Japan
Ishimura, Kimihiro, Tokyo, Japan

Ohtani, Yoshiro, Tokyo, Japan
Kimura, Kunio, Tokyo, Japan
Fujii, Masahiro, Tokyo, Japan
Hata, Yoshiyuki, Tokyo, Japan
PA Kaken Pharmaceutical Co., Ltd., Japan (non-U.S. corporation)
PI US 5482929 960109
AI US 92-996392 921223 (7)
PRAI JP 91-357821 911226
DT Utility
EXNAM Primary Examiner: Warden, Jill; Assistant Examiner: Salata, Carol A.
LREP Rosenman & Colin
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A composition of a stabilized fibroblast growth factor (FGF), which contains an aluminum salt of cyclodextrin sulfate to stabilize FGF. FGF can be stabilized by forming a composition of FGF and an aluminum salt of cyclodextrin sulfate, and can be stably prepared into formulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 23 OF 30 USPATFULL
AN 95:96677 USPATFULL
TI Ink-jet ink and method of printing using the same
IN Yui, Toshitake, Minami-ashigara, Japan
Yamashita, Yoshiro, Minami-ashigara, Japan
Koide, Fuminori, Minami-ashigara, Japan
Chujo, Akihiko, Minami-ashigara, Japan
Hashimoto, Ken, Minami-ashigara, Japan
PA Fuji Xerox Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 5462590 951031
AI US 94-184195 940118 (8)
DCD 20120711
PRAI JP 93-27124 930125
DT Utility
EXNAM Primary Examiner: Klemanski, Helene
LREP Oliff & Berridge
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 622
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An ink-jet ink contains water, a coloring material and an amine compound represented by the formula: R.sub.1 R.sub.2 R.sub.3 N (I) wherein one or two of R.sub.1, R.sub.2 and R.sub.3 represent(s)

(an) alkyl group(s) having 1 to 5 carbon atoms substituted by at least one group selected from the group consisting of a carboxy group, a sulfonic acid group, and a Li, Na, Na, K or ammonium salt thereof, and the remainder represents(s) (an) hydrogen atom(s) or (an) alkyl group(s) having 1 to 5 carbon atoms substituted by a hydroxide group or a carbamoyl group. The pH value of the ink is preferably between 6 to 8. Moreover, printing may be made by applying thermal energy to the ink and forming droplets.

The ink and the method of printing using the ink may prevent the change of the amount of ink droplets due to kogation on a heater even with a long-term use, and may not cause a heater trouble due to the corrosion of materials constantly in contact with ink. Further, even if the ink is stored for a long-period, the pH of the ink may be kept to be stable and clogging of print head may be prevented and change of hue of images may be avoided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 24 OF 30 USPATFULL
AN 95:73625 USPATFULL
TI Substituted cyclodextrin sulfates and their uses as growth modulating agents
IN Weisz, Paul B., State College, PA, United States
Ewing, William R., King of Prussia, PA, United States
Joullie, Madeleine M., Philadelphia, PA, United States
PA The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PI US 5441944 950815
AI US 92-947417 920918 (7)
DCD 20080528
RLI Continuation of Ser. No. US 91-691168, filed on 24 Apr 1991, now abandoned which is a continuation of Ser. No. US 89-397559, filed on 23 Apr 1989, now abandoned
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Duane, Morris & Heckscher
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 712
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to highly water soluble substituted .alpha.-, .beta.- or .gamma.-cyclodextrin sulfates associated with a physiologically acceptable cation. Pathological or otherwise undesirable cell or tissue growth in mammals, including humans, is inhibited by administering thereto (1) a water-**soluble** substituted **cyclodextrin** sulfate **salt**, together with (2) a growth-inhibiting organic compound. The

growth-inhibiting compound (2) may be asteroid having no inhibiting effect in the absence of (1), or an organic compound which may be an active growth inhibitor, the action of which is potentiated by (1). The invention provides a method for inhibiting angiogenesis and controlling the growth of tumors as well as treating other diseases and pathological conditions associated with undesired cell or tissue growth, including angiogenesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 25 OF 30 USPATFULL
AN 94:55568 USPATFULL
TI Compositions and methods for drug delivery and chromatography
IN Lincoln, Stephen F., Stonyfell, Australia
Coates, John H., North Adolaide, Australia
Easton, Christopher J., Bellevue Heights, Australia
Van Eyk, Stephen J., Ludwigshafen, Germany, Federal Republic of
May, Bruce L., Tranmere, Australia
Singh, Paramjit, Queensland, Australia
Williams, Michael L., Brompton, Australia
Stile, Martyn A., Parkside, Australia
PA Australia Commercial Research & Development Limited, Brisbane, Australia (non-U.S. corporation)
PI US 5324750 940628
AI US 92-979451 921120 (7)
RLI Continuation of Ser. No. US 91-684888, filed on 12 Apr 1991, now abandoned
PRAI AU 88-165 880831
AU 88-189 880901
AU 88-618 880927
AU 88-1053 881019
AU 88-1198 881027
AU 88-1417 881111
AU 89-4894 890626
AU 89-4909 890626
AU 89-5034 890703
AU 89-5278 890717
AU 89-5354 890719
AU 89-5576 890803
AU 89-5641 890807
AU 89-5682 890809
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Foley & Lardner
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 2807
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cyclodextrin derivatives and inclusion complexes having increased solubility and stability are provided. Cyclodextrin derivatives include amino and other modified cyclodextrins, and linked cyclodextrins. Inclusion complexes comprising the foregoing cyclodextrins, and processes for making the cyclodextrin derivatives are disclosed. Also disclosed are cyclodextrin derivatives comprising otherwise substituted or unsubstituted cyclodextrins covalently bonded to agents such as pharmaceuticals. The covalent bond, when broken, yields the agent in active form. Pharmaceutical compositions and methods of treating an animal host are also described, as well as chromatographic compositions and a method for separating racemic mixtures.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 26 OF 30 USPATFULL
AN 94:26524 USPATFULL
TI Inclusion complexes of 3-morpholino-sydnonimine or its salts or its tautomer isomer, process for the preparation thereof, and pharmaceutical compositions containing the same
IN Vikmon, Maaria, Budapest, Hungary
Szejtli, Jozsef, Budapest, Hungary
Szente, Lajos, Budapest, Hungary
Gaal, Jozsef, Budapest, Hungary
Hermecz: Istvan, Budapest, Hungary
Horvath, Agnes, Budapest, Hungary
Marmarosi, Katalin, Biatorbagy, Hungary
Horvath, Gabor, Budapest, Hungary
Munkacsi, Iren, Budapest, Hungary
PA Chinoin Gyogyszer- ES Vegyeszeti Termekek Gyara Rt., Budapest, Hungary (non-U.S. corporation)
PI US 5298496 940329
AI US 92-793389 920102 (7)
WO 91-HU13 910328
920102 PCT 371 date
920102 PCT 102(e) date
PRAI HU 90-1869 900328
HU 90-1869 900627
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Dubno, Herbert; Myers, Jonathan
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 553
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to inclusion complexes of 3-morpholino-sydnonimine or its salts or its tautomer isomer, process for the preparation thereof and pharmaceutical

compositions containing the same.

The inclusion complex of 3-morpholino-sydnonimine or its salt formed with cyclodextrin derivative is prepared by

a) reacting the 3-morpholino-sydnonimine or its salt in an aqueous medium with a cyclodextrin derivative and the complex is isolated from the solution by dehydratation, or

b) high energy milling of 3-morpholino-sydnonimine or its salt and a cyclodextrin derivative.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 27 OF 30 USPATFULL
AN 93:87328 USPATFULL
TI (Quinolin-2-ylmethoxy)indole/cyclodextrin complex
IN Kwong, Elizabeth, Pointe Claire, Canada
PA Merck Frosst Canada, Inc., Quebec, Canada (non-U.S. corporation)
PI US 5254541 931019
AI US 91-793059 911115 (7)
DT Utility
EXNAM Primary Examiner: Waddell, Frederick E.; Assistant Examiner: Hook, Gregory
LREP DiPrima, Joseph F.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A complex of cyclodextrin and 3-[N-(p-chlorobenzyl)-3-(t-buthylthio)-5-(quinolin-2-ylmethoxy)indol-2-yl]-2,2-dimethylpropanoic acid, sodium salt is more soluble in water than the sodium salt alone. The complex is useful as an anti-asthmatic, anti-allergic, anti-inflammatory, or cytoprotective agent. It is also useful in treating diarrhea, hypertension, angina, platelet aggregation, cerebral spasm, premature labor, spontaneous abortion, dysmenorrhea, and migraine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 28 OF 30 USPATFULL
AN 91:42702 USPATFULL
TI Growth inhibiting agent and the use thereof
IN Folkman, Moses J., Brookline, MA, United States
Weisz, Paul B., Yardley, PA, United States
PA The Trustees of the University of Pennsylvania/Childrens Hospital Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 5019562 910528

AI US 89-434659 891109 (7)
RLI Continuation of Ser. No. US 89-295638, filed on 10 Jan 1989, now abandoned which is a continuation-in-part of Ser. No. US 88-145407, filed on 19 Jan 1988, now abandoned
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Pennie & Edmonds
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1056
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Pathological or otherwise undesirable cell or tissue growth in mammals, including humans, is inhibited by administering thereto a composition exemplified by (1) a water-**soluble** **cyclodextrin** sulfate **salt**, together with (2) a growth-inhibiting organic compound. The growth-inhibiting compound (2) may be a steroid having no inhibiting effect in the absence of (1), or an organic compound which may be an active growth inhibitor, the action of which is potentiated by (1). The invention provides a method for inhibiting angiogenesis and controlling the growth of tumors as well as treating other diseases and pathological conditions associated with undesired cell or tissue growth, including angiogenesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 29 OF 30 USPATFULL
AN 84:59836 USPATFULL
TI Complex compounds
IN Shinoda, Masamitu, Minou, Japan
Tanaka, Ikuo, Minou, Japan
Yasuda, Tadahiko, Kyoto, Japan
Nakajima, Isao, Toyonaka, Japan
Adachi, Tutomu, Itami, Japan
Ikeda, Giichi, Kyoto, Japan
PA Teikoku Chemical Industry Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4478995 841023
AI US 82-412972 820827 (6)
PRAI JP 81-138048 810901
DT Utility
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 180
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A complex of an acid addition salt of (2'-benzyloxycarbonyl)phenyl trans-4-guanidinomethylcyclohexanecarboxylate and a cyclodextrin. The complex is useful for the treatment of ulcers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L12 ANSWER 30 OF 30 USPATFULL
AN 81:24626 USPATFULL
TI Suds suppressing compositions and detergents containing them
IN Gandolfo, Daniel, Levallois Perret, France
Cooper, David J., Wezembeek-Oppem, Belgium
PA The Procter & Gamble Company, Cincinnati, OH, United States (U.S. corporation)
PI US 4265779 810505
AI US 79-72254 790904 (6)
PRAI GB 78-36242 780909
DT Utility
EXNAM Primary Examiner: Willis, Jr., P. E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 823
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Storage stable, particulate suds suppressing compositions containing a liquid hydrocarbon, a nonionic ethoxylate and a compatibilizing agent capable of forming inclusion compounds are disclosed. In addition to the liquid hydrocarbon, the suds suppressing compositions frequently comprise additional suds suppressing agents such as silica and/or solid waxes. Granular detergents containing the particulate suds suppressing compositions and a method of enhancing the efficacy of liquid hydrocarbon suds regulants are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his l13-; d 1-32 bib abs

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGLAUNCH, DRUGB, CEN, CIN, CBNB' ENTERED AT 11:11:56 ON 19 NOV 1998)
L13 106 S L11
L14 38 S L13 AND INCLUSION
L15 32 DUP REM L14 (6 DUPLICATES REMOVED)

L15 ANSWER 1 OF 32 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
Searcher : Shears 308-4994

AN 98-480917 [41] WPIDS
DNC C98-145496
TI New **inclusion** complex in aqueous solution - contains 3,4-di aryl-chroman and cyclodextrin, useful for treating bone loss.
DC A96 B02
IN RASMUSSEN, S R
PA (NOVO) NOVO-NORDISK AS
CYC 80
PI WO 9837884 A1 980903 (9841)* EN 17 pp
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
ADT WO 9837884 A1 WO 98-DK73 980225
PRAI DK 97-216 970227
AN 98-480917 [41] WPIDS
AB WO 9837884 A UPAB: 981014
An **inclusion** complex in aqueous solution comprises a compound of formula (I) or a **salt**, and a water-**soluble cyclodextrin**.
USE - The **inclusion** complex is useful for inhibiting bone loss (claimed). It can be used to treat e.g. osteoporosis, Paget's disease, hyperparathyroidism, and hypercalcemia of malignancy, and other conditions.
ADVANTAGE - (I) and their salts are poorly water-soluble and, as pharmaceutical agents, have disadvantages associated with poor water-solubility. The present aqueous solutions overcome these disadvantages.
Dwg.0/0

L15 ANSWER 2 OF 32 TOXLIT
AN 1998:61678 TOXLIT
DN CA-128-248567R
TI Method of selecting **salts** with desired **solubility** in aqueous **cyclodextrin** solution for manufacture of **inclusion** complexes.
AU Kim IS
SO (1998). Jpn. Kokai Tokkyo Koho PATENT NO. 9859871 03/03/1998 (Pfizer Inc.).
CODEN: JKXXAF.
CY UNITED STATES
DT Patent
FS CA
LA Japanese
OS CA 128:248567
EM 199805
AB In selecting (pharmaceutical) salts having soly. in aq. cyclodextrin

soln. equal to or greater than a target soly. (set by doses required for therapeutic efficacy), a series of salts are obtained, their equil. soly. in the aq. soln. is measured, then their soly. is compared with the target one. The soly. of ziprasidone tosylate, tartrate, mesylate, etc., in aq. .beta.-cyclodextrin sulfobutyl ether was measured, and the mesylate was selected as the most desirable salt.

L15 ANSWER 3 OF 32 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 98-020733 [03] WPIDS
DNC C98-007764
TI Comparing **solubilities** of **salts** of a compound in aqueous **cyclodextrin** - to target a particular **salt** or **salts** having a **solubility** equal to or greater than a desired solubility.
DC B04 B07
IN KIM, Y
PA (PFIZ) PFIZER INC; (PFIZ) PFIZER CORP
CYC 18
PI EP 811386 A2 971210 (9803)* EN 11 pp
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
JP 10059871 A 980303 (9819) 9 pp
ADT EP 811386 A2 EP 97-302821 970424; JP 10059871 A JP 97-115720 970506
PRAI US 96-16866 960507
AN 98-020733 [03] WPIDS
AB EP 811386 A UPAB: 980119
A method of locating one or more salts of a compound, the **salts** having a **solubility** in a **cyclodextrin** equal to or greater than a desired **solubility**, comprises obtaining a series of **salts** of the compound, determining the equilibrium **solubility** of each **salt** in the series in an aqueous solution of the **cyclodextrin**, and comparing each measured solubility with the target solubility.

Also claimed is a method of determining a useful salt from within a series of salts of a particular medicinal compound, for use in making a composition of matter comprising the salt and a **cyclodextrin**, the series of **salts** is obtained, their equilibrium **solubility** in aqueous **cyclodextrin** solution is determined, and a **salt** in the series having a **solubility** equal to or greater than the desired target solubility is selected as the useful salt.

USE - Used for selecting a salt for making an **inclusion** complex.

Dwg.0/1

L15 ANSWER 4 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-42502 DRUGU P G
TI Binding, uptake, and transport of hypericin by Caco-2 cell

monolayers.

AU Sattler S; Schaefer U; Schneider W; Hoelzl J; Lehr C M

CS Univ.Saarland; Univ.Marburg; Steigerwald

LO Saarbruecken, Marburg; Darmstadt, Ger.

SO J.Pharm.Sci. (86, No. 10, 1120-26, 1997) 11 Fig. 1 Tab. 32 Ref.
CODEN: JPMSAE ISSN: 0022-3549

AV Department of Biopharmaceutics and Pharmaceutical Technology, University of the Saarland, P.O. Box 15 11 50, 66041 Saarbruecken, Germany. (C.M.L.). (email:lehr@rz.uni-sb.de).

LA English

DT Journal

FA AB; LA; CT

FS Literature

AN 97-42502 DRUGU P G

AB **Inclusion** complexation of hypericin (HY) in alpha-**cyclodextrin** (alpha-CD), beta-1,8-CD, gamma-CD, beta-1-O-acetyl-CD (all Wacker), 2-hydroxypropyl-beta-CD (HPCD, Roquette-Freres), and beta-CD-sulfobutylether 7-Na **salt** (Cydex) enhanced its aqueous **solubility**. The in-vitro transfer of HY across Caco-2 monolayers from HY-HPCD complexes was temperature-dependent and HY-HPCD was bound or internalized by the cells. Free HY did not permeate Caco-2 cells but was bound to non-specific surface receptors. Although HY **solubility** was increased by incorporation into liposomes made from lecithin and phosphatidic acid (Phospholipon-80, Rhone-Poulenc-Rorer), liposomal HY did not permeate the cell layers.

ABEX The **solubility** of HY in pN 7.4 PBS was increased from 40 to between 100 and 200 ug/ml by increasing concentrations of CD (1-5%). The **solubility** profile exhibited negative curvature and was best fitted to type A(N). Respective permeation of HY-HPCD **inclusion** complexes across Caco-2 cell layers on polycarbonate supports was 3.22 and 0.12% at 37 deg and 4 deg in 5 hr, membrane binding was 23.81 and 5.39%, and apparent permeability constants were 1.274 and 0.048 x 10 power minus 6 cm/sec. Only 60-70% of HY leaving the donor compartment was transported from the apical to the basolateral side of the cells due to extensive internalization or binding. Non-complexed HY was extensively bound to the surface of Caco-2 cells by non-specific, low affinity receptors: Kd values were 181 and 136 uM at 37 and 4 deg, respectively.Although NY was **solubilized** by incorporation into liposomes (400-900 ug/ml), in this form it did not permeate Caco-2 cells and was fully recovered from the donor compartment. (S62/WS)

L15 ANSWER 5 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD

AN 97-20023 DRUGU G

TI Study of the influence of both **cyclodextrins** and L-lysine on the aqueous **solubility** of nimesulide; isolation and characterization of nimesulide-L-lysine-**cyclodextrin**

complexes.
AU Piel G; Pirotte B; Delneuville I; Neven P; Llabres G; Delarge J; Delattre L
CS Univ.Liege
LO Liege, Belg.
SO J.Pharm.Sci. (86, No. 4, 475-80, 1997) 6 Fig. 3 Tab. 20 Ref. CODEN: JPMSAE ISSN: 0022-3549
AV Laboratoire de Technologie Pharmaceutique, Institut de Pharmacie, rue Fusch 5, 4000 Liege, Belgium.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 97-20023 DRUGU G
AB Both complexation of nimesulide (NM, Stragen) with beta-**cyclodextrin** (BCD, CNI) prepared according to patent application WO 94/02177 and preparation of its L-lysine (Janssen) **salt** greatly increased the aqueous **solubility** of NM. The effects of BCD, gamma-**cyclodextrin** (GCD, Wacker), and L-lysine on the **solubility** of NM were evaluated. **Inclusion** complexes NM-Lys-BCD and NM-Lys-GCD showed enhanced aqueous **solubility**.
ABEX NM-Lys-BCD and NM-Lys-GCD complexes were prepared by spray-drying. **Inclusion** complexation of the NM-Lys **salt** was confirmed by differential scanning calorimetry and PMR spectra. NM determination at 97 nm and Karl Fischer water analysis showed a stoichiometry of 1:1:1 for the complexes. **Solubility** of 1 g NM in 20 ml aqueous solutions of 10 mM BCD, 50 mM GCD, 100 mM Lys, 10 mM BCD + 100 mM Lys, and 50 mM GCD + 100 mM Lys were 0.025, 0.022, 4.450, 6.590, and 19.070 mg/ml, respectively. The respective aqueous **solubility** of NM at pH 1.5, 6.8, and purified water was 0.005, 0.015, and 0.01 mg/ml, for the NM-Lys-BCD complex was 0.048, 2.373, and 36.400 mg/ml, and for the NM-Lys-GCD complex was 0.023, 1.711, and 33.600 mg/ml. (WS)

L15 ANSWER 6 OF 32 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 96-388693 [39] WPIDS
DNN N96-327415 DNC C96-122530
TI **Cyclodextrin** contg. water-soluble dyes - comprise **cyclodextrin** and slightly water-**soluble** metal complex **salt** dye.
DC E21 G02 T04
PA (MITQ) MITSUBISHI ELECTRIC CORP; (ORIE-N) ORIENT KAGAKU KOGYO KK
CYC 1
PI JP 08188722 A 960723 (9639)* 9 pp
ADT JP 08188722 A JP 95-18749 950110
PRAI JP 95-18749 950110
AN 96-388693 [39] WPIDS
AB JP08188722 A UPAB: 970129

Water-soluble dye comprises (b) **cyclodextrin** including (a) a slightly water-**soluble** metal complex **salt** dye of formula (I) where A, A' = diazo component residue of mono- or di-halogen or nitro-substd. o-aminophenol or anthranilic acid; B, B'= coupling component residue of opt. amino- or -NHCOR- substd. beta-naphthol or a pyrazolone deriv. with R = 1-4 C alkyl; M = di- or tri-valent metal; X = -O-, or -COO- Ka = alkali metal or NH4. Also claimed are a mfr. of water-soluble dyes and water-based ink compsns. contg.. the water-soluble dyes.

The water-soluble dye pref. has a wt. ratio of (a) : (b) of 1 : 1 - 1 : 10. (a) is typically of C.I. Solvent Violet 21 and C.I. Solvent Red 8.

USE - The water-soluble dyes are useful for writing instruments, inks for ink jet recording, stamp and printing inks and stains for woodworking.

ADVANTAGE - The water-soluble dyes contain substantially no inorganic salts deteriorating ink stability and have a high **inclusion** rate, high solubility in water contributing to a high colouring power and excellent dissolution stability in aq. solvents and light resistance.

Dwg.0/2

L15 ANSWER 7 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 96-24706 DRUGU G
TI Nimesulide-L-lysine-beta- and gamma-**cyclodextrin** complexes: Preparation and dissolution properties.
AU Piel G; Pirotte B; Delneuville I; Neven P; Delarge J; Delattre L
LO Liege, Belg.
SO J.Pharm.Belg. (51, No. 2, 117, 1996) 1 Tab.
CODEN: JPBEAJ ISSN: 0047-2166
AV Laboratoire de Technologie Pharmaceutique, Institute de Pharmacie, rue Fusch 3-5, B-4000 Liege, Belgium.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 96-24706 DRUGU G
AB Nimesulide (NI) is a NSAID poorly **soluble** in water (0.01 mg/ml). Beta-**cyclodextrin** (beta-CD) can increase the aqueous **solubility** of the NI up to 16 mg/ml (patent WO94/02177). The formation of a nimesulide-L-lysine **salt** (NI-Lys) can also increase the NI aqueous **solubility** up to 5.0-7.5 mg/ml (PCT/BE95/00055). The present study investigated the interaction of both CDs and L-lysine (Lys) on the aqueous **solubility** of NI. (conference abstract).
ABEX Phase **solubility** studies showed that the **solubility** of the NI-Lys **salt** increases linearly with the concentration of CD (AL diagram type according to Higuchi and Connors). The apparent stability constants (K) for the NI-Lys

with beta- and gamma-CD were 67.04 M-1 and 111.7 M-1, respectively. NI-Lys-beta- and gamma-CD complexes in the stoichiometric ratio (1:2:1) were prepared by spray-drying. The **inclusion** of the NI-Lys **salt** into the CD cavity was proven by DSC and 1H-NMR. These complexes presented good aqueous **solubility** characteristics. (PH)

L15 ANSWER 8 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 97-05370 DRUGU P G
TI Hypericin-**cyclodextrin** formulations for improved delivery and **solubility** of hypericin.
AU Sattler S; Schaefer U; Schneider W; Hoelzl J; Lehr C M
LO Marburg; Darmstadt, Ger.
SO Pharm.Res. (13, No. 9, Suppl., S328, 1996)
CODEN: PHREEB ISSN: 0724-8741
AV Dept. of Pharm. Biology, 35032 Marburg, Germany.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 97-05370 DRUGU P G
AB With an optimized buffer system, it was possible to study the epithelial transport and binding of naphthodianthrone hypericin (HYP) and any interaction between 2-hydroxypropyl beta-**cyclodextrin** and HYP using filter grown Caco-2 cell monolayers. The saturation **solubility** of HYP in water was greatly enhanced with the addition of **cyclodextrin** .These data are indicative for conformational changes of HYP under influence of **cyclodextrins** rather than the formation of **inclusion** complexes. Comparing 6 different **cyclodextrins**, there was no difference in **solubility** behaviour, except for a beta-**cyclodextrin**-sodium **salt**, there the HYP **solubility** decreases by higher **cyclodextrin** -concentration. (conference abstract).
ABEX Methods Both the pharmaceutical formulation and the biological evaluation of HYP in various test models is seriously hampered by the very poor water **solubility** of this compound. HYP was extracted from Hypericum perforatum, characterized and purified up to a purity greater than 93%, noticed that aqueous **solubility** decreases by higher purity. As the **solubility** of HYP is strongly influenced by mono- and divalent ions, an isoosmotic aqueous buffer system with lower ion-concentrations, resulting in an improved HYP **solubility** , was developed as a physiological medium for cell culture studies. The interaction between 2-hydroxypropyl-beta-**cyclodextrin** and HYP was investigated on the basis of phase **solubility** analysis. Results The saturation **solubility** of HYP in water was enhanced from 40 ug/ml up to 480 ug/ml under addition

of 30% **cyclodextrin**, which is approx. equal to the **solubility** of HYP in methanol. The molar ratios of HYP and 2-hydroxypropyl-beta-**cyclodextrin** were in the order of 1:100. The differential UV/VIS spectra of 0.079 mmol/l HYP in water in the presence of 0.79-395 mmol/l 2-hydroxypropyl-**cyclodextrin** showed a shift of the aqueous HYP spectrum towards the methanolic spectrum. Comparing 6 chemically different **cyclodextrins**, there was no great difference in **solubility** behaviour, except for a beta-**cyclodextrin**-sodium **salt**, there the HYP **solubility** decreases by higher **cyclodextrin** concentration, respectively, sodium concentration. (NR)

L15 ANSWER 9 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-32433 DRUGU P G E S
TI The effect of SBE4-beta-CD on i.m. prednisolone pharmacokinetics and tissue damage in rabbits: Comparison to a co-solvent solution and a water-**soluble** prodrug.
AU Stella V J; Lee H K; Thompson D O
CS Univ.Kansas
LO Lawrence, Kans., USA
SO Int.J.Pharm. (120, No. 2, 197-204, 1995) 5 Fig. 2 Tab. 28 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS 66045, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 95-32433 DRUGU P G E S
AB The bioavailability of prednisolone (PD, Sigma-Chem.) was similar when given i.m. to rabbits in a cosolvent mixture (PEG 400 (Aldrich)/ethanol/water) or a solution of **inclusion** complex with sulfobutyl ether derivative variably substituted on the 2-, 3- and 6-positions of beta-**cyclodextrin** (SBE4-b-CD), but slightly lower from a prodrug (PD 21-phosphate 2Na, Steroidals) in saline. Muscle damage (changes in plasma creatine kinase (CK) levels), was minimal from SBE4-b-CD or NaCl but greater from cosolvent, independent of the presence of PD. The results confirm that i.m. drugs such as PD are rapidly, quantitatively and safely released from SBE4-b-CD **inclusion** complexes and that SBE4-b-CD may provide an alternative to cosolvents or prodrugs for i.m. delivery of sparingly water-**soluble** drugs such as PD.
ABEX Methods Male New Zealand White rabbits (mean 4.4 kg) received i.m. 5 mg/kg PD dissolved in PEG 400/ethanol/water 40:10:50 or in 0.09 M SBE4-b-CD solution, or PD 21-phosphate ester 2Na **salt** in 0.68% NaCl solution, or cosolvent, 0.9 M SBE4-b-CD or normal saline alone, in randomized cross-over design. PD was

assayed by HPLC. Results In rabbits given i.m. solutions without PD, the AUC for change in plasma CK levels over 24 hr post-injection was higher for the cosolvent (mean 79 U.hr/ml) than 0.09M SBE4-b-CD (11 U.hr/ml) or normal saline (14 U.hr/ml) which did not differ. The slight elevation in plasma CK seen with SBE4-b-CD and saline were attributed to tissue damage caused by venous punctures, as plasma CK levels increased with number of plasma samples taken in rabbits not given i.m. solutions. In rabbits given PD-containing cosolvent, SBE4-b-CD and prodrug solutions, the CK AUC to 24 hr was 51, 7.7 and 9.7 U.h/ml, respectively; CK AUC values were similar with vs. without PD for saline/prodrug or SBE4-b-CD solutions but was lower for PD in cosolvent than blank cosolvent, possibly due to local anti-inflammatory action of PD. PD in cosolvent or SBE4-b-CD, or prodrug solution, produced mean plasma concentration AUC of 0.76, 0.94 and 0.15 ug.min/ml, with mean Cmax of 4.58, 6.45 and 6.16 ug/ml at Tmax of 0.41, 0.47 and 0.32 hr, declining with half-life of 2.5, 1.5 and 1.6 hr, respectively. The bioavailability of PD relative to that from cosolvent was 87% from SBE4-b-CD and 78% from the prodrug. (W103/DAC)

L15 ANSWER 10 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD

AN 95-37974 DRUGU P G E

TI Enhancement of dissolution rate and hypoglycemic activity of glibenclamide with beta-**cyclodextrin**.

AU Babu R J; Pandit J K

CS Univ.Banaras-Hindu

LO Varanasi, India

SO STP Pharm.Sci. (5, No. 3, 196-201, 1995) 8 Fig. 31 Ref. ISSN: 1157-1489

AV Department of Pharmaaceutics, Institute of Technology, Banaras Hindu University, Varanasi 221 005, India. (J.K.P.).

LA English

DT Journal

FA AB; LA; CT

FS Literature

AN 95-37974 DRUGU P G E

AB Glibenclamide (GB, Hoechst) formed an **inclusion** complex with beta-**cyclodextrin** (BCD, SD-Fine-Chem.) in solution and in the solid state. **Inclusion** complexation was confirmed by IR spectroscopy, X-ray diffraction, and differential scanning calorimetry. **Inclusion** complexation enhanced the aqueous **solubility** of GB. In streptozocin diabetic rats, p.o. GB-BCD complex gave an enhanced hypoglycemic effect compared with p.o. GB.

ABEX Methods Phase **solubility** was studied at RT, and GB was determined spectrophotometrically at 229 nm. GB and GB-BCD were suspended in 1% NaCMC and given p.o. to fasted male albino rats (120-160 g) with diabetes induced by 25 mg/kg i.p.

streptozotocin. Results There was a 3-fold increase in the **solubility** of GB-BCD compared with GB. The dissolution rates of GB-BCD **inclusion** complex and a kneaded mixture at 20 min were 8 and 7 times higher, respectively, than the pure drug. In diabetic rats, p.o. 1 mg GB equivalent/kg of **inclusion** complex and the kneaded mixture had a greater hypoglycemic effect at 4, 6, and 8 hr, compared with the same dose level of GB. The hypoglycemic response/AUC of p.o. 1 mg GB equivalent/kg as **inclusion** complex and the kneaded mixture was 1.5- and 1.4-fold greater, respectively, than that of GB. At 0.7 mg GB equivalent/kg, the **inclusion** complex and kneaded mixture produced a similar hypoglycemic effect as that of 1 mg/kg of pure GB. (WS)

L15 ANSWER 11 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-32432 DRUGU P G E
TI The effect of SBE4-Beta-CD on i.v. methylprednisolone pharmacokinetics in rats: Comparison to a co-solvent solution and two water-**soluble** prodrugs.
AU Stella V J; Lee H K; Thompson D O
CS Univ.Kansas
LO Lawrence, Kans., USA
SO Int.J.Pharm. (120, No. 2, 189-95, 1995) 3 Fig. 2 Tab. 21 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Department of Pharmaceutical Chemistry, The University of Kansas, Lawrence, KS 66045, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 95-32432 DRUGU P G E
AB The pharmacokinetic parameters of methylprednisolone (MP, Sigma-Chem.) in rats were similar when given i.v. in either a cosolvent mixture (PEG 400 (Aldrich)/ethanol/water) or solution of **inclusion** complex with sulfobutyl ether derivative variably substituted on the 2-, 3- and 6-positions of beta-**cyclodextrin** (SBE4-b-CD), but lower AUC was achieved from i.v. water-**soluble** prodrugs of MP (MP 21-phosphate ester disodium **salt** (Upjohn), or MP 21-hemisuccinate ester monosodium **salt**, Sigma-Chem.). The results confirm that i.v. drugs such as MP are rapidly and quantitatively released from SBE4-b-CD **inclusion** complexes and suggest that modified **cyclodextrins** such as SBE4-b-CD may provide an alternative to co-solvents or prodrugs for the parenteral delivery of sparingly water-**soluble** drugs such as MP.
ABEX Methods Male Sprague-Dawley rats (mean 291 g) received i.v. 20 mg/kg MP or MP equivalents, as MP dissolved in PEG 400/ethanol/water (60:12:28) or 0.075 M SBE4-b-CD solution, or i.v. aqueous solutions of MP prodrugs. Plasma MP was assayed by HPLC.

Results MP given in cosolvent or SBE4-b-CD solutions produced similar mean values for extrapolated AUC (326.7 vs. 317.4 ug.min/ml), half-life (41.5 vs. 43.2 min), clearance (62.7 vs. 63.8 ml/min/kg) area under moment curve (0.0149 vs. 0.0132 ug.sq.min/ml) or mean residence time (42 vs. 41.5 min, respectively). The prodrugs also produced similar half-life and only slightly longer mean residence times, but lower extrapolated AUC values. As a result, the absolute bioavailability of MP (AUC relative to that from cosolvent) was 97.1% from SBE4-b-CD, vs. 59.2% and 33.2% from aqueous solutions of MP 21-phosphate and MP 21-hemisuccinate, respectively. (W103/DAC)

L15 ANSWER 12 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-17347 DRUGU P G V
TI Novel liposome-based multicomponent systems for the protection of photolabile agents.
AU Loukas Y L; Jayasekera P; Gregoriadis G
CS Univ.London
LO London; Porton Down, U.K.
SO Int.J.Pharm. (117, No. 1, 85-94, 1995) 2 Fig. 4 Tab. 23 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Centre for Drug Delivery Research, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX, England. (G.G.).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 95-17347 DRUGU P G V
AB Riboflavin 5'-monosodium **salt** (R, FMN, Aldrich) and its complexes with beta-**cyclodextrin** (BCD) or gamma-**cyclodextrin** (CCD) (both Wacker) were incorporated into dehydration-rehydration multilamellar vesicles (DRV) made with egg phosphatidylcholine (PC, lecithin), 1-alpha-distearoyl phosphatidylcholine (DSPC) (both Lipids-Products) and cholesterol (CH, Sigma-Chem.) together with lipid-**soluble** photoprotectants Oil Red O (RO), oxybenzone (OB), dioxybenzone (DB) or water-**soluble** sulisobenzone (SB) and beta-carotene (BC) (all Sigma-Chem.). UV photodegradation of R in DVR was decreased by RO but the greatest photoprotection was obtained using liposomal R-CCD combined with RO, OB, DB and BC.
ABEX Methods R, R-BCD or R-CCD (0.004 mmol) were incorporated into DRV made from PC, DSPC and CH (0.04 mmol) with or without photoprotectants alone (0.008 mmol) or in combination (0.002-0.008 mmol). Selected DRV were exposed to UV light (365 nm; 460 uW/sq.cm/decimetre) and half-lives of R were measured. Results The high entrapment efficiency of R in DRV (41%-47%) was unaffected by lipid-**soluble** RO, OB and DB (entrapment efficiencies 98%, 96% and 95%) but was reduced by water-**soluble** SB (to

25%) and a combination of all photoprotectants (27%). The entrapment of R-BCD and R-CCD complexes (21%-23% and 19%-21%) was unchanged by lipid-**soluble** photoprotectants but the latter was reduced by **inclusion** of BC (8%-19%). The half-life of R in UV light (0.48 hr) was increased by entrapment in DRV (1.92 hr) and was further enhanced by RO (31.22 hr). The halflife of the R-CCV complex (2.9 hr) was increased by **inclusion** into DRV (9.63 hr) and was further increased to 82.5, 105 and 128.33 hr by RO combined with OB and DB, and with OB, DB and BC, respectively. (JC)

L15 ANSWER 13 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-30668 DRUGU G
TI Influence of beta-**cyclodextrin** on the rheological and mucoadhesive properties of polysaccharides intended for ophthalmic use.
AU Ganzerli G; Verschueren E; Ludwig A
CS Univ.Antwerp
LO Antwerp, Belg.
SO ; Pharm.World Sci. (17, No. 3, Suppl. H, H6, 1995)
CODEN: ; PWSC
AV Department of Pharmaceutical Sciences, University of Antwerp (UIA), 2610 Antwerp (Wilrijk), Belgium.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 95-30668 DRUGU G
AB A major disadvantage of eye drops is their rapid drainage after instillation, resulting in the poor bioavailability of ophthalmic solutions. One way of prolonging the residence time in the pre-corneal area consists of adding viscous agents. In order to improve the absorption of poorly water **soluble** drugs **inclusion** complexes with **cyclodextrins** were proposed. This study demonstrated no influence of beta-**cyclodextrin** on the rheological and mucoadhesive properties of polysaccharides intended for ophthalmic use: sodium alginate, sodium carboxymethylcellulose, scleroglucan, hydroxyethylcellulose, xanthan gum and carragheenin. (conference abstract).
ABEX Various polymer solutions were prepared in an iso-osmotic mannitol vehicle, with or without added beta-**cyclodextrin**. The rheological behavior was evaluated from viscosity measurements carried out with a rotational viscometer at 32 deg. To assess mucin-polysaccharide interactions, the method proposed by Hassan and Gallo was followed. The index of mucoadhesion was calculated from rheological data obtained after dilution of the polysaccharide solutions with simulated lacrimal fluid. Scleroglucan and xanthan gum exhibited a strong pseudoplastic behavior, while the other polymers showed an approximately Newtonian flow. The addition of

beta-**cyclodextrin** had no significant influence on the rheological properties of the polysaccharides at the concentrations used. Scleroglucan, sodium carboxymethylcellulose, hydroxyethylcellulose, sodium alginate and xanthan gum possessed mucoadhesive properties. On the contrary, carragheenin showed a negative index of mucoadhesion. The presence of several concentrations of beta-**cyclodextrin** did not interfere with the mucin-polysaccharide interactions. (PH)

L15 ANSWER 14 OF 32 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 95-022724 [03] WPIDS
DNC C95-010547
TI New complexes of nimesulide **salts** with **cyclodextrin**(s) - have improved **solubility**, used as antiinflammatory and antipyretic agents.
DC B04 B05
IN GECZY, J; CECZY, J
PA (CYCL-N) CYCLOLAB LTD; (EURO-N) EUROPHARMACEUTICALS SA; (CYCL-N) CYCLOLAB CIKLODEXTRIN KUTATO FEJLESZTO; (CYCL-N) CYCLOLAB CYCLODEXTRIN RES & DEV LAB LTD
CYC 43
PI WO 9428031 A1 941208 (9503)* EN 18 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU BG BR BY CA CN CZ FI JP KP KR KZ LV MN NO NZ PL RO RU SI SK UA US UZ VN
AU 9470813 A 941220 (9512)
FI 9500294 A 950124 (9516)
NO 9500243 A 950313 (9519)
EP 656015 A1 950607 (9527) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
HU 68239 T 950628 (9532)
HU 210922 B 950928 (9545)
CZ 9500163 A3 951018 (9549)
JP 07509498 W 951019 (9550) 10 pp
AU 675146 B 970123 (9712)
US 5744165 A 980428 (9824) 10 pp
EP 656015 B1 980826 (9838) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE SI
DE 69412760 E 981001 (9845)
ADT WO 9428031 A1 WO 94-HU14 940518; AU 9470813 A AU 94-70813 940518, WO 94-HU14 940518; FI 9500294 A WO 94-HU14 940518, FI 95-294 950124; NO 9500243 A WO 94-HU14 940518, NO 95-243 950123; EP 656015 A1 EP 94-919796 940518, WO 94-HU14 940518; HU 68239 T HU 93-1518 930524; HU 210922 B HU 93-1518 930524; CZ 9500163 A3 CZ 95-163 940518; JP 07509498 W WO 94-HU14 940518, JP 95-500436 940518; AU 675146 B AU 94-70813 940518; US 5744165 A WO 94-HU14 940518, US 95-374765 950321; EP 656015 B1 EP 94-919796 940518, WO 94-HU14 940518; DE 69412760 E DE 94-612760 940518, EP 94-919796 940518, WO 94-HU14 940518

Searcher : Shears 308-4994

FDT AU 9470813 A Based on WO 9428031; EP 656015 A1 Based on WO 9428031; HU 210922 B Previous Publ. HU 68239; JP 07509498 W Based on WO 9428031; AU 675146 B Previous Publ. AU 9470813, Based on WO 9428031; US 5744165 A Based on WO 9428031; EP 656015 B1 Based on WO 9428031; DE 69412760 E Based on EP 656015, Based on WO 9428031
PRAI HU 93-1518 930524
AN 95-022724 [03] WPIDS
AB WO 9428031 A UPAB: 950126
Inclusion complexes of nimesulide alkali and alkaline earth metal salts with cyclodextrins and cyclodextrin derivatives are new. The salts have the formula (I) where A is the metal ion equivalent.

USE - Nimesulide is a known anti-inflammatory and antipyretic agent. It has very poor aq. solubility but the present complexes have improved solubility and faster gastro intestinal absorption resulting in higher plasma levels.
Dwg.0/3

L15 ANSWER 15 OF 32 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 93:352995 SCISEARCH
GA The Genuine Article (R) Number: LE817
TI SYNTHESIS AND PROPERTIES OF 6A-AMINO-6A-DEOXY-ALPHA AND 6A-AMINO-6A-DEOXY-BETA-CYCLODEXTRIN
AU BROWN S E; COATES J H; COGHLAN D R; EASTON C J (Reprint); VANEYK S J; JANOWSKI W; LEPORE A; LINCOLN S F; LUO Y; MAY B L; SCHIESSER D S; WANG P; WILLIAMS M L
CS UNIV ADELAIDE, DEPT CHEM, GPO BOX 498, ADELAIDE, SA 5001, AUSTRALIA
CYA AUSTRALIA
SO AUSTRALIAN JOURNAL OF CHEMISTRY, (1993) Vol. 46, No. 6, pp. 953-958. ISSN: 0004-9425.
DT Note; Journal
FS PHYS
LA ENGLISH
REC Reference Count: 20
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The monotosylates obtained by treatment of alpha- and beta-cyclodextrin with p-methylbenzenesulfonyl chloride reacted with ammonia to give the title compounds. These amines are of unusually low basicity, with pK(a) values of 8.70 and 8.72, respectively. In water at 25-degrees, the hydrochloride salt of the amine derived from beta-cyclodextrin is approximately 40 times more soluble than beta-**cyclodextrin** and, through complexation, the **salt** increases the **solubility** of Nabumetone over 800 times.

L15 ANSWER 16 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 93-20834 DRUGU P T S G V
TI Preparation and Evaluation of Dermatological Formulations Based on **Inclusion** of Tretinoin in Beta-**Cyclodextrin** and

Hydroxypropyl-Beta-**Cyclodextrin**.

AU Rolland A; Shroot B
LO Valbonne, France

SO J.Invest.Dermatol. (100, No. 2, 219, 1993) 4 Ref.
CODEN: JIDEAE ISSN: 0022-202X

AV Centre International de Recherches Dermatologiques (CIRD) Galderma, Sophia Antipolis, Valbonne, France.

LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 93-20834 DRUGU P T S G V

AB To improve the **solubility** and stability of tretinoin in aqueous topical dosage forms and reduce its skin irritation potency whilst maintaining its therapeutic efficacy, **inclusion** complexes of tretinoin in beta-**cyclodextrin** or hydroxypropyl beta-**cyclodextrin** were prepared. Tretinoin water **solubility** was increased by the complexes, and with tretinoin triethanolamine **salt**. An aqueous gel containing tretinoin/beta-**cyclodextrin inclusion** complex was as effective as a commercial gel (Aberel) in the topical treatment of patients with acne vulgaris and had reduced irritation. **Cyclodextrins** may protect drugs from oxidation, photodecomposition and improve their therapeutic index by reducing side-effects or modifying drug bioavailability. (congress abstract).

ABEX **Inclusion** complexes of tretinoin in either beta-**cyclodextrin** or hydroxypropyl beta-**cyclodextrin** were prepared. Tretinoin **solubility** in water was increased by **inclusion** in beta-**cyclodextrin** and hydroxypropyl beta-**cyclodextrin** by about 400 and 5000x, respectively, and a further augmentation was obtained by using the tretinoin triethanolamine **salt**. Aqueous solutions containing **inclusion** complexes of tretinoin with beta-**cyclodextrin** or hydroxypropyl beta-**cyclodextrin**, jellified with Carbopol (tretinoin final concentration: 0.025%), were stable for 2 mth at 45 deg and for 2 yr at 20 deg. These gels were less irritant than commercial formulations of tretinoin in a rabbit skin irritancy test. Although the profiles of in-vitro tretinoin release from the **cyclodextrin** drug delivery systems were different from those of commercial formulations, in-vitro drug penetration kinetics through hairless rat or human skin were found to be similar. An aqueous gel containing tretinoin/beta-**cyclodextrin inclusion** complex presented a comedolytic activity at least equivalent to that of a commercial hydroalcoholic gel (Aberel 0.025%) in the rhino mouse model. This aqueous gel was also as effective as the commercial formulation in the topical treatment of patients with acne vulgaris and was better tolerated with in particular reduced irritation.

Cyclodextrins enhanced the **solubility** of lipophilic drugs in water, permitting the use of totally aqueous formulations. (DAC)

L15 ANSWER 17 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 92-20388 DRUGU G
TI Complexation of Dihydropyridine Derivatives with **Cyclodextrins** and 2-Hydroxypropyl Beta-**Cyclodextrin** in Solution.
AU Mueller B W; Albers E
CS Byk-Gulden
LO Kiel, Constance, Germany,West
SO Int.J.Pharm. (79, No. 2-3, 273-88, 1992) 10 Fig. 4 Tab. 25 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Dept. of Pharmaceutics, Christian Albrecht University, Gutenbergstr. 76-78, D-2300 Kiel 1, Germany.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 92-20388 DRUGU G
AB Structure-interaction relationships in the **inclusion** complexation of beta-**cyclodextrin** (beta-CD), 2-hydroxypropyl beta-CD (HP-BCD), (both Chinoin), gamma-CD, and alpha-CD with various 1,4-dihydropyridines (DHP) including nitrendipine (NP), nimodipine (NM), and nisoldipine (NS) (all Bayer) were studied on the basis of phase **solubility** analysis, stabilization effects, and PMR spectrometry. Also, the influence of HP-BCD on the adsorption of DHP on PVC injection sets (Original-Infusomat tube, Braun-Melsungen), and the compatibility of the complex with excipients (saline injection, bovine serum, dextran, fructose, xylitol, glucose, sorbitol, propylene glycol (PG), oxypolygelatin) used in i.v. injectable solutions were evaluated.
ABEX The interaction of DHP (determined by HPLC) with CD decreased in the order beta-CD, HP-BCD, gamma-CD, alpha-CD. The **solubilization** of DHP with HP-BCD was strongly influenced by pH and the counterion, indicating a considerable influence of the degree of dissociation of the guest molecule on complex formation. DHP with aromatic substitution were more strongly **solubilized** than those with alkyl esters such as NP. The intensity of interaction of HP-BCD with DHP was dependent on aromatic substituents and decreased in the order (I), (II), (III) = (IV). **Solubilization** by HP-BCD decreased in the order NS, NM, NT, and was slight, whereas for the aromatic DHP it was more effective and decreased in the order (I), (II), (III), (+)-(IV), (-)-(IV), NT. The 4-(3-nitrophenyl)-DHP were photolabile, and were not stabilized by complexation with HP-BCD. HP-BCD had a destabilizing effect on the chemical stability of DHP.

Searcher : Shears 308-4994

Formulations of 10% PG and HP-BCD in 0.02 M potassium phosphate buffer were passed through the PVC infusion sets. Adsorption of DHP on PVC was markedly reduced by complexation with HP-BCD. The addition of 20% human albumin led to complete recovery of the drug. The compatibility of 1.33 mg (-)-(IV) in 10% HP-BCD was enhanced compared with conventionally **solubilized** systems, and was improved by excipients in decreasing order hexoses or sugar alcohols, dextran, physiological saline, BSA, and modified gelatin. (WS)

L15 ANSWER 18 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 93-24553 DRUGU G
TI Albumin Microspheres and Betacyclodextrin **Inclusion** Complex Containing Diclofenac Sodium.
AU Devi S G; Prakasam K; Udupa N
LO Bangalore, Manipal, India
SO Indian J.Pharm.Sci. (54, No. 6, 259-61, 1992) 1 Tab. 4 Ref.
CODEN: IJSIDW ISSN: 0250-474X
AV Dept. of Pharmaceutics, Al-Ameen College of Pharmacy, Bangalore, India.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 93-24553 DRUGU G
AB Diclofenac Na (DC) was formulated as microspheres using cross-linked egg albumin and hydroxypropyl methylcellulose (HPMC). **Inclusion** complexation of the DC using beta-**cyclodextrin** (BC) led to enhanced DC entrapment efficiency and release rate but reduced the diffusion of the drug across dialysis membranes.
ABEX Methods DC:albumin (300 mg each) in 2 ml water was added to 2.5, 5, or 7.5% HPMC (15 cps) in chloroform. After mixing, 1.5 ml 25% glutaraldehyde was added and homogenized for 3 hr; 5 ml 1M glycine was added and the mixture was further stirred for 1 hr. The mixture was centrifuged and washed to obtain the microspheres. Results Entrapment efficiency of free DC and DC-BC complex in albumin microspheres containing 2.5% HPMC was 52.4 and 99.7%, respectively. DC release rates through dialysis membrane in 6 hr at pH 7.6 from microspheres containing 2.5% HPMC and free DC or DC-BC complex were 85.6 and 27.2%, respectively. Release rates of DC in 3 hr at pH 7.6 from microspheres containing 2.5% HPMC and free or DC-BC complex were 27.5 and 46.8%, respectively. (WS)

L15 ANSWER 19 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 91-37630 DRUGU P G E
TI Effect of Hydrotropic Substances on the Complexation of Sparingly **Soluble** Drugs with **Cyclodextrin** Derivatives and the Influence of **Cyclodextrin** Complexation on the

Pharmacokinetics of the Drugs.

AU Mueller B W; Albers E
CS Byk-Gulden
LO Kiel, Constance, Germany,West

SO J.Pharm.Sci. (80, No. 6, 599-604, 1991) 6 Fig. 3 Tab. 25 Ref.
CODEN: JPMSAE ISSN: 0022-3549

AV Department of Pharmaceutics, Christian Albrecht University, Gutenbergstr. 76-78, D-2300 Kiel 1, Germany.

LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 91-37630 DRUGU P G E

AB Methyltestosterone (MeT, Schering-Berlin) **solubility** in aqueous 2-hydroxypropyl-beta-**cyclodextrin** (HP-CD; Chinoin) solutions was decreased by increasing sorbitol (Karion) but was increased by urea (both Merck-Darmstadt) and nicotinamide (NSA; Roche). 1,2-Propylene glycol (1,2-PG, BASF) and Na deoxycholate (DOC, Fluka) displaced MeT from HP-CD **inclusion** complexes. The hypotensive effects of i.v. 3-(2-(-)-(4-chlorobenzyl)- pyrrolidinyl-1)-propyl ester (DHP-I) in SHR were similar when given in PEG or HP-CD. The pharmacokinetics of i.v. 3-(4,4-diphenyl piperidinyl-1)-propyl ester (DHP-II) (both Byk-Gulden) in dogs as HP-CD and 1,2-PG formulations were similar but p.o. in dogs and monkeys were enhanced by HP-CD complexation.

ABEX Methods MeT (200 mg) was stirred with H2O (10 ml) together withHP-CD (1-10%) and either sorbitol (5-50%), urea or NSA (both 50%), DOC or 1,2-PG (1-5%). SHR were given DHP-1 (0.1 umol/kg) in 10% PEG or HP-CD (at 0.2 ml/min). Beagle dogs were given 1 mg/kg i.v. DHP-II in either 1,2-PG or HP-CD. Beagle dogs and cynomolgus monkeys were given DHP-II (10 and 30 mg/kg p.o., respectively) formulated with 1,2-PG in soft gelatin capsules or as HP-CD complex in aqueous solution.Plasma drug levels were measured by HPLC. Results The **solubility** of MeT in HP-CD (8 mg/ml in 6% HPCD) was increased by 50% urea and NSA (to 10 and 22 mg/ml) and was depressed by 10-50% sorbitol (to 6 mg/ml). Enhanced **solubility** due to NSA was due to entropy effects (water structure disruption) and possibly to complex formation with MeT.Addition of NSA to MeT in HP-CD enhanced its **solubility** when NSA exceeded 2 mol/l. In SHR, the fall in B.P. in response to DHP-I was 30% in PEG or HP-CD and returned to baseline over 300 min. Serum levels in dogs were similar and declined monoexponentially after i.v. DHP-II in 1,2-PG or HP-CD. Given p.o. peak plasma DPH-II levels in dogs and monkeys were greater after complex in HP-CD than in 1,2-PG (87.9 and 171.2 vs. 75.5 and 29.1 ng/ml, respectively) and occurred after similar times (1.5-8 hr). Absolute p.o. bioavailability was increased by the HP-CD formulation (13 and 6.19 vs. 8 and 0.9%). (S62/WS)

L15 ANSWER 20 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 91-42014 DRUGU P G
TI Effect of Enhancers on Cutaneous Permeation of Piroxicam In-Vitro. (Chinese).
AU Xu G Q; Xi N Z; Chen G S; Jiang X G; Xu H N
LO Shanghai, Hangzhou, China
SO Acta Pharmacol.Sin. (12, No. 3, 235-38, 1991) 1 Fig. 2 Tab. 11 Ref. CODEN: CYLPDN ISSN: 0253-9756
AV Division of Biopharmaceutics, Shanghai Medical University, Shanghai 200032, China. (Xi N.Z.).
LA German
DT Journal
FA AB; LA; CT
FS Literature
AN 91-42014 DRUGU P G
AB Flux of piroxicam (PX) through the skin of hairless BALB/CAnN mice (8-10 wk-old, 23.2 g) in-vitro was greatly enhanced by 1% azone (Nelson) alone (factor of 21.4) or with 20% propylene glycol (PG) (25.2-fold). It was enhanced by 3.2-4.6-fold by 10% ethyl acetate, 5% oleate and 20% ethanol, or when presented as a beta-**cyclodextrin inclusion** complex. Little effect (0.9-2.1-fold enhancement) was seen with 10% dimethylsulfoxide (DMSO), 30% polyethylene glycol (PEG 400), 20% PG, 10% acetone, or urea or salicylic acid (both 1%). **Solubility** of PX at 37 deg was 73 mg/ml in DMSO, 15-24 mg/ml in acetone, ethyl acetate or PEG 400, 2-9 mg/ml in azone, oleate or ethanol, and 0.46-0.52 mg/ml in PG or saline.
ABEX (YC)

L15 ANSWER 21 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 92-03611 DRUGU G
TI Stability Studies on Steroidal Drug/beta-**Cyclodextrin** Kneaded Systems.
AU Torricelli C; Martini A; Muggetti L; Eli M; De Ponti R
CS Farmitalia-Erba
LO Milan, Italy
SO Int.J.Pharm. (75, No. 2-3, 147-53, 1991) 6 Fig. 2 Tab. 5 Ref. CODEN: IJPHDE ISSN: 0378-5173
AV New Drug Delivery Systems Section, Galenical R & D, Farmitalia Carlo Erba srl, 24 via Imbonati, I 20159, Italy.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 92-03611 DRUGU G
AB 6-Methylenandrosta 1,4-diene-3,17-dione (FCE-24304; Farmitalia-Erba) formed an **inclusion** complex with beta-**cyclodextrin** (CD; Spad-Roquette) in which the drug degradation rate was slow. The dissolution rate of FCE-24304 was

increased by formation of the complex and was relatively unchanged on storage. The **inclusion** complex was readily tableted using Na starch glycolate (Mendell), microcystalline cellulose (FMC) and Mg stearate (Framitalia-Erba).

ABEX Methods FCE-24304 and CD (1:1 and 1:2) were kneaded together with water for 30 min, dried at 35 deg and sieved. Tablets (230 mg) with hardness of 4.3 kp and were prepared from the 1:2 product (193.7 mg) with CD (6.3 mg), starch glycolate (17.7 mg), microcrystalline cellulose (10 mg) and Mg stearate (2.3 mg). Dissolution rates were measured by USP-XXII No. 2 at pH 7.4 and 37 deg and FCE-24304 determined spectrophotometrically at 250 nm. Results Thermal and X-ray analysis of FCE-24304:CD (1:2) demonstrated complete disappearance of crystalline drug as a result of the formation of the **inclusion** complex. In the 1:1 product approximately 50% of FCE-24304 remained as the crystalline product. The residual crystallinity was unchanged after 3 mth storage at 35 deg but was decreased at 55 deg (21 vs. 44%) with a significant increase in by-products (6.81 vs. 1.05%). The 1:2 product was stable to storage at 55 deg and 35 deg with 80% relative humidity (1.99 and 0.92% by-products). 73 And 91% FCE-24304 was dissolved from 1:1 and 1:2 products in 10 min and these rates were unchanged by prolonged storage. The 1:2 tablets had a hardness of 43 kp and disintegration time of 2 min. (S62/WS)

L15 ANSWER 22 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 91-48679 DRUGU G
TI Interaction of NSA with **Cyclodextrins** and Hydroxypropyl **Cyclodextrin** Derivatives.
AU Backensfeld T; Mueller B W; Kolter K
CS Knoll
LO Kiel, Ludwigshafen, Germany,West
SO Int.J.Pharm. (74, No. 2-3, 85-93, 1991) 9 Fig. 2 Tab. 19 Ref.
CODEN: IJPHDE ISSN: 0378-5173
AV Dept. of Pharmaceutics and Biopharmacy, Christian Albrecht University, Gutenbergstr. 76-78, D-2300 Kiel, Germany.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 91-48679 DRUGU G
AB The effects of **inclusion** complexation with hydroxyalkylated **cyclodextrins** (CD) on the **solubility** and stability of diclofenac Na (DC, Synopharm), piroxicam (PC, Schwarz), and indomethacin (IN, Helm) were studied. Hydroxypropyl-beta-CD (HP-beta-CD, Janssen), HP-gamma-CD, and beta-CD (Chinoin) had **solubilizing** activity on DC, PC and IN. Unlike DC and IN, CD had a destabilizing effect on PC. Computer models of the IN and DC complexes were derived based on PMR data.

Searcher : Shears 308-4994

ABEX The stability constants of the IN complexes calculated from the slope and intercept of the phase **solubility** graph were larger in the non-ionized form, whereas the number of mol IN/mol CD was more marked in basic media. The pH profile of IN at 21 and 41 deg showed 4 straight lines, indicating that HP-beta-CD did not change the degradation reaction of IN. However, at both temperatures, HP-beta-CD reduced IN hydrolysis by 50%. The influence of beta-CD and HP-beta-CD on the stability of DC solutions with and without oxygen at 71 deg was determined: after 207 days, the amount of DC undegraded in solution without oxygen and with HP-beta-CD and beta-CD as stabilizers was 34.6 and 30.4%, respectively. At RT, the decrease was not significant, even when solutions without CD were physically unstable due to recrystallization of CD. All CD acclerated the rate of decomposition of PC: the destabilizing effect was in decreasing order HP-gamma-CD, beta-CD, HP-beta-CD. (WS) (B.W.M.).

L15 ANSWER 23 OF 32 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 1
AN 90:433175 BIOSIS
DN BA90:93976
TI HIGH-FIELD NMR TECHNIQUES FOR THE INVESTIGATION OF A BETA CYCLODEXTRIN INDOMETHACIN **INCLUSION** COMPLEX.
AU DJEDAINI F; LIN S Z; PERLY B; WOUESSIDJEWE D
CS LAB. PHARM. GALENIQUE BIOPHARM., UA CNRS 1218, 5 RUE JEAN BAPTISTE CLARMENT, F-92296 CHATENAY MALABRY CEDEX, FR.
SO J PHARM SCI 79 (7). 1990. 643-646. CODEN: JPMSAE ISSN: 0022-3549
LA English
AB The **inclusion** complex of indomethacin sodium salt in .beta.-cyclodextrin has been studied by proton NMR at high magnetic field. The continuous variation technique was used to evidence the formation of a soluble 1:1 complex in aqueous solution of physiological pH. The effective association constant was determined by the Benesi-Hildebrand procedure to be 760 M-1 at 303 K. This technique requires NMR measurements in the presence of a very large excess of one of the complex components and, since both .beta.-**cyclodextrin** and the sodium **salt** of indomethacin are sparingly **soluble** in water, NMR spectrometers operating at very high magnetic fields were used. Besides the effective association constant, the Benesi-Hildebrand approach allows a precise determination of all NMR parameters of the pure **inclusion** complex which may be used for a complete analysis of the geometry of this complex in solution.

L15 ANSWER 24 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 90-07822 DRUGU P E G
TI Pharmacokinetics of Dexamethasone After Intravenous Administration of an **Inclusion** Complex in beta-Hydroxypropyl-**Cyclodextrin**.
AU Dietzel K; Estes K S; Brewster M E; Bodor N S; Derendorf H

LO Gainesville, Florida, United States
SO Pharm.Res. (6, No. 9, Suppl., 131, 1989) ISSN: 0724-8741
AV College of Pharmacy, University of Florida, JHMHC- Box 494, Gainesville, FL 32610, U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 90-07822 DRUGU P E G
AB In a crossover study, 6 mongrel dogs were i.v. injected with dexamethasone (DEX) either as the sodium **salt** of the phosphate ester or as a water-**soluble inclusion** complex in beta-hydroxypropyl- **cyclodextrin** (HPCD). The HPCD form of DEX had a greater initial bioavailability, and pharmacokinetic data confirmed that HPCD may be a suitable vehicle for the i.v. administration of poorly water **soluble** drugs like DEX. There were no toxic effects. (congress abstract).
ABEX DEX (5 mg/kg) was administered in a crossover design to 6 mongrel dogs either as the sodium **salt** of the phosphate ester or a water **soluble inclusion** complex in HPCD. Plasma and urine were collected and assayed for DEX using HPLC. Pharmacokinetic analysis showed that the administration of the HPCD **inclusion** complex resulted in a significantly higher AUC during the first hr (1.73 +/- 0.12 vs. 0.91 +/- 0.20 ug/hr/ml) indicating a higher initial bioavailability. Renal clearance was increased when given with HPCD (1.14 +/- 0.10 vs. 0.48 +/- 0.18 ml/min/kg). (E54/RSV)

L15 ANSWER 25 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 89-04800 DRUGU P G
TI The Effect of **Inclusion** in **Cyclodextrins** on the Absorption of Dantrolene.
AU Poelma F G J; Hilbers H W; Jansen A C A; Tukker J J
LO Utrecht, Netherlands
SO Pharm.Weekbl. Sci.Ed. (10, No. 6, 293, 1988) 1 Ref.
CODEN: PWSEDI ISSN: 0167-6555
AV Dept. of Pharmaceutics, University of Utrecht, Croesestraat 79, 3522 AD Utrecht, The Netherlands.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 89-04800 DRUGU P G
AB The effect of **inclusion** of alpha, beta and gamma **cyclodextrins** on **solubility** and transfer of dantrolene sodium (DA) across the isolated rat intestinal wall was studied. **Cyclodextrins** did enhance the **solubility** of DA in the order beta more than alpha and alpha more than gamma. When **cyclodextrins** were added to

the perfusion solution, the absorption rate of DA was reduced proportionally to the reduction of the concentration of free DA. Apart from the reduction of free DA by complex formation, no clear influence of CD on the transport process of the drug across the intestinal wall could be seen. (congress abstract).

ABEX In the present study it was investigated whether besides an enhanced **solubility** by **inclusion** in CD, transfer of the drug across the intestinal wall was altered in the presence of CD. In this study, DA, a poorly water-**soluble** lipophilic drug with low bioavailability, was used as a model compound. The **inclusion** of DA in alpha, beta, gamma **cyclodextrins** was determined by a **solubility** method. **Cyclodextrins** did enhance the **solubility** of DA, beta more than alpha and alpha more than gamma. Based on the **solubility** data the fraction of DA free in solution was calculated according to the phase separation model. In this model the free fraction of the drug and the fraction bound to CD are considered as 2 separate phases. Subsequently, the influence of **cyclodextrins** on the absorption of DA was investigated in a chronically isolated internal loop in the small intestine of the rat. Absorption kinetics of DA were evaluated on the basis of disappearance rates of the drug from the luminal perfusion solution. When **cyclodextrins** were added to the perfusion solution, the absorption rate of DA was reduced proportionally to the reduction of the concentration of free DA (phase-separation). Apart from the reduction of free DA by complex formation, no clear influence of CD on the transport process of the drug across the intestinal wall could be seen. (PM)

L15 ANSWER 26 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 89-05649 DRUGU E G
TI Buccal Administration of a Brain-Targeted Redox-Based Chemical Delivery System for Estradiol in Rats.
AU Estes K S; Derendorf H; Brewster M E; Bodor N
LO Gainesville, Florida, United States
SO Pharm.Res. (5, No. 10, Suppl., S100, 1988) ISSN: 0724-8741
AV Center Drug Design and Delivery, College of Pharmacy, University of Florida, Gainesville, FL 32610, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 89-05649 DRUGU E G
AB The redox-based brain-targeted system for drug delivery which is based on in vivo conversion of a lipophilic dihydropyridine carrier to the corresponding hyrophilic **salt** carrier was applied to estradiol (E2-CDS) and i.v. administered in a water **soluble** 2-hydroxypropyl- beta-**cyclodextrin** **inclusion** complex to ovariectomized (OVX) rats. Other rats

received E2-CDS via buccal, rectal, gavage or intragastric routes. Effects on body weight gain (BWG), serum LH, estradiol (E2) and oxidized drug levels (E2-Q+) were compared. The results demonstrated good brain delivery after i.v. and buccal administration of E2-CDS. Thus, E2-CDS may be successfully formulated for buccal or sublingual administration as a **cyclodextrin inclusion** complex. (congress abstract).

ABEX OVX rats were treated i.v. with a dose (2 mg/kg) previously shown to decrease BWG, decrease serum LH, and increase brain oxidized drug levels (E2-Q+) without elevating circulating E2 at 12 days post-treatment. 4 Other groups of rats were treated via buccal (8 mg/kg), rectal (8 mg/kg), gavage (feeding needle, 20 mg/kg) or intragastric (20 mg/kg) administration routes. BWG was suppressed only in the i.v. and buccal dosing groups over the course of the study. Serum LH values were also significantly decreased in the 2 groups but did not significantly differ among the other 3 groups. Brain E2-Q+ levels were consistently elevated 12 days post-treatment after i.v. dosing (127 +/- 12 ng/g) and similar after buccal treatment (90 +/- 22 ng/g). However, brain levels were undetectable in 19/24 rats in other treatment groups. (E54/RSV)

L15 ANSWER 27 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 88-11731 DRUGU P E G
TI Comparing Administration Routes for a Novel Redox-Based Chemical Delivery System for Estradiol.
AU Estes K S; Brewster M E; Derendorf H; Mullersman G; Bodor N
LO Gainesville, Florida, United States
SO J.Pharm.Sci. (76, No. 11, S169, 1987)
CODEN: JPMSAE ISSN: 0022-3549
AV Ctr. for Drug Design and Delivery, College of Pharmacy, Univ. of Florida, Gainesville, Florida, U.S.A.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 88-11731 DRUGU P E G
AB S.c., p.o. and i.v. administration of a redox type brain directed chemical drug delivery system for estradiol (CDS-E2), based on in-vivo conversion of a lipophilic dihydropyridine drug carrier to the corresponding hydrophilic **salt** carrier, were compared in rats. 24 Hr after 5 mg/kg CDS-E2 i.v. in a water-**soluble** 2-hydroxypropyl beta-**cyclodextrin** (CD) **inclusion** complex or in DMSO brain drug levels were 0.8 ug/ml; s.c. CDS-E2 at the same dose in sesame oil gave 30% of these levels. Brain specific delivery of E2 was supported by significant pharmacological activity after 3 wk with basal serum E2 levels. Administration of 20 mg/kg CDS-E2 in aqueous CD by gavage gave

increased brain drug levels (1.4 ug/g); direct intragastric treatment gave low levels (0.05 ug/g). S.c. or p.o. administration were thus effective. (congress abstract).

ABEX (HR)

L15 ANSWER 28 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 86-46673 DRUGU P G
TI Studies on **Inclusion** Complexes of Non-steroidal Anti-inflammatory Agents with Cyclophosphorase-A.
AU Okada Y; Horiyama S; Koizuml K
LO Nishinomiya, Japan
SO J.Pharm.Soc.Jpn. (106, No. 3, 240-47, 1986) 6 Fig. 4 Tab. 15 Ref.
CODEN: YKKZAJ ISSN: 0031-6903
AV Faculty of Pharmaceutical Sciences, Mukogawa Women's University, 4-16 Edagawa-cho, Nishinomiya, 663, Japan.
LA Japanese
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 86-46673 DRUGU P G
AB Cyclosophoraoses (CS) are unbranched cyclic (1-2)-beta-D-glucans (degree of polymerization 17-40) produced by many strains of Agrobact. and Rhizobium. CS have a larger cavity depth and diameter than the **cyclodextrins** and are more water-**soluble** . **Inclusion** complexes of CS with flurbiprofen (FP), indomethacin (IM), mefenamic acid (MA), and phenylbutazone (PB) were investigated, compared with those produced with beta-**cyclodextrin** (BC). CS had no hemolytic activity on human RBC, and reduced the hemolytic activity of FP and IM.

ABEX CS-A (glucose units 17, mol. weight 2754) were used, and the **solubility** technique was applied by different methods. **Inclusion** complexes were obtained when CS-A and NSAID were dissolved in aqueous ammonia, and the mixture was lyophilized. The complex had a ratio of NH3:drug of about 1, and it was assumed that the NSAID was in the form of the NH4 **salt** and was stabilized by CS-A. NSAID content was determined by HPLC. **Solubilities** (mM) of uncomplexed FP, IM, MA and PB, were 0.27 +/- 0.20, 1.01 +/- 0.80, 0.11 +/- 0.25, and 0.13 +/- 0.0, respectively; with CS-A, values were 2.25 +/- 0.97, 3.05 +/- 0.85, 2.01 +/- 0.96, and 2.12 +/- 0.85, respectively. BC gave values of 4.75 +/- 0.63, 3.76 +/- 0.82, 3.78 +/- 0.86, and 2.70 +/- 0.81, respectively. (WS)

L15 ANSWER 29 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 86-25371 DRUGU P
TI Effect of Beta-**Cyclodextrin** on Sleeping Time Induced by Barbituric Acid Derivatives in Mice.
AU Shirakura O; Nambu N; Nagai T
LO Tokyo, Japan

SO Chem.Pharm.Bull. (33, No. 8, 3517-21, 1985) 3 Fig. 2 Tab. 21 Ref.
CODEN: CPBTAL ISSN: 0009-2363
AV Faculty of Pharmaceutical Sciences, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 86-25371 DRUGU P
AB In mice, the sleeping times induced by i.v. or i.p. hexobarbital (HB), pentobarbital Na (PB) (both Tokyo Kasei), phenobarbital (PH, Fujinaga) and thiopental Na (TP, Ravonal; Tanabe) were shortened by co-administration of beta-**cyclodextrin** (CD, Nihon-Shokuhin-Kako). This may have been the result of decreased distribution to the brain as a result of complex formation between barbiturates and CD with depressed membrane permeability.
ABEX Methods Male ddY mice (20-26 g) were treated with HB, PB, PH orTP (50, 47.9, 49.1, 51.3 mg/kg) i.v. or i.p. with or without CD (215.3 umol/kg). At the time of awakening, blood and brain barbiturate levels were determined by HPLC. HB was incubated with rat serum in phosphate buffer pH 7.4 for 1 day at 22 deg. Levels of solvent-extractable HB were assayed. Results The sleeping times induced by HB, PB and TP i.v. were significantly shortened by i.v. CD but sleeping lags were unchanged. At the time of awakening, brain BA levels were unaltered by CD, although whole blood concentrations were increased. The sleeping lags induced by i.p. barbiturates were prolonged by CD and sleeping times were significantly shortened. The **solubility** of HB in rat plasma was lower than in buffer but was increased with increasing concentrations of CD as a result of formation of an **inclusion** complex. (S62/WS)

L15 ANSWER 30 OF 32 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 2
AN 86:13093 BIOSIS
DN BR30:13093
TI EFFECT OF **CYCLODEXTRINS** ON SPARINGLY **SOLUBLE SALTS**.
AU HIRSCH W; FRIED V; ALTMAN L
CS CHEM. DEP., BROOKLYN COLL., CITY UNIV. NEW YORK, BROOKLYN, N.Y. 11210.
SO J PHARM SCI 74 (10). 1985. 1123-1125. CODEN: JPMSAE ISSN: 0022-3549
LA English

L15 ANSWER 31 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 83-25805 DRUGU C
TI Effect of Water-**Soluble** Beta-**Cyclodextrin** Polymer on the Lipophilicity of Polymyxine Examined by Reversed-Phase Thin-Layer Chromatography.
AU Cserhati T; Bordas B; Fenyvesi E; Szejtli J

CS Chinoin
LO Budapest, Hungary
SO J.Chromatogr. (259, No. 1, 107-10, 1983) 1 Fig. 2 Tab. 14 Ref.
CODEN: JOCRAM ISSN: 0378-4347
AV Research Institute for Plant Protection, Budapest, Hungary.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 83-25805 DRUGU C
AB A TLC study showing that beta-**cyclodextrin** forms **inclusion** complexes with the antibiotic polymyxin (Pfizer), reducing its lipophilicity and adsorption energy on silica gel is reported. The biological activity of a compound is dependent upon its lipohilicity and adsorption energy.
ABEX Polymyxin was dissolved in distilled water. The water **soluble** polymer of beta-**cyclodextrin** was prepared by cross linking with epichlorohydrin. The eluent used was water/ethanol containing Li, Na, Mg, K **salts**. Lipophilicity studies were carried out by reversed phase TLC on Kieselgel G plates impregnated with paraffin oil in hexane. Samples were spotted on the lower part of a plate. The adsorption strength was measured on non-impregnated plates. After development the plates were dried and polymyxin detected by ninhydrin. The exact Rf values were determined by video -densitometer. At constant organic solvent ratio and **salt** nature the interaction between the 2 compounds became weaker with increasing **salt** concentration. A lower dielectric constant of the solution counteracted the complex formation. The beta-**cyclodextrin** caused a reduction in the lipophilicity of polymyxin and its adsorption energy on silica gel.

L15 ANSWER 32 OF 32 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 94-46506 DRUGU M G
TI Effect of interaction of drug-beta-**cyclodextrin** with bile **salts** on the drug absorption from small intestine.
AU Nakanishi K; Masukawa T
CS Univ.Setsunan
LO Osaka, Japan
SO Can.J.Physiol.Pharmacol. (72, Suppl. 1, 211, 19
CODEN: CJPPA3 ISSN: 0008-4212
AV Department of Clinical Biochemistry, Faculty of Pharmaceutical Sciences, Setsunan University, Hirakata, Osaka, Japan.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AN 94-46506 DRUGU M G
AB Beta-**cyclodextrin** (Beta-CyD) forms **inclusion**

complex with hydrophobic drugs, resulting in the improvement of **solubility**, dissolution rate and bioavailability of the drug, and its complex is also used to avoid the irritation to gut. The interaction of bile-acids and beta-CyD (native), methyl-beta-CyD (**cyclodextrin**-beta-permethyl), hydroxyethyl-beta-CyD, hydroxypropyl-beta-CyD and sulfamethizole (SMZ)-beta-CyD complex were investigated in rats. Bile **salts** were found to act as competing agents in the GI tract. However, the modified beta-CyDs revealed somewhat different behavior to bile **salts** in comparison with that of native beta-CyD. The interaction of beta-CyD complex with bile **salts** in the intestinal lumen plays an important role in the drug absorption from p.o. drug-beta-CyD complexes. (conference abstract).

ABEX CyDs used in this study were beta-CyD (native) and a part of modified beta-CyD such as, methyl-beta-CyD, hydroxyethyl-beta-CyD and hydroxypropyl-beta-CyD. The absorption of SMZ after dosing SMZ-beta-CyD complex was determined by a closed loop method with or without bile. The blood level of SMZ after dosing SMZ-beta-CyD complex in bile ligated rat was significantly decreased in comparison with that of SMZ alone, and the modified beta-CyDs were also similar effects. The blood level of SMZ after dosing SMZ-beta-CyD complex in intact rat or bile ligated rat with sodium cholate (SC) was recovered the same level as in the case of SMZ alone. Therefore, bile **salts** were found to act as competing agents in the GI tract. However, the modified beta-CyDs revealed somewhat different behavior to bile **salts** in comparison with that of native beta-CyD. (AE)

=> d his l16-; d 1-7 bib abs

(FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, TOXLIT, TOXLINE, DRUGU, DRUGNL, DRUGLAUNCH, DRUGB, CEN, CIN, CBNB, USPATFULL' ENTERED AT 11:17:02 ON 19 NOV 1998)

Author

L16 43566 S KIM Y?/AU
L17 822 S L16 AND (L2 OR SALT)
L18 9 S L17 AND (L1 OR CYCLODEXTRIN OR CYCLO DEXTRIN)
L19 7 DUP REM L18 (2 DUPLICATES REMOVED)

L19 ANSWER 1 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1
AN 1997:745974 CAPLUS
DN 128:39555
TI Inclusion complexes of aryl heterocyclic **salts**
IN Johnson, Kevin Charles; **Kim, Yesook**; Shanker, Ravi Mysore
PA Pfizer Inc., USA; Johnson, Kevin Charles; Kim, Yesook; Shanker, Ravi

Searcher : Shears 308-4994

Mysore
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
PI WO 9741896 A2 19971113
DS W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 97-IB321 19970401
PRAI US 96-19204 19960507
DT Patent
LA English
OS MARPAT 128:39555
AB Compns. comprise a pharmaceutically acceptable **salt** of an aryl heterocyclic compd., such as ziprasidone, in a **cyclodextrin**. Preferred **cyclodextrins** are .beta.-**cyclodextrin** sulfbutyl ether (SBECD) and hydroxypropyl .beta.-**cyclodextrin** (HPBCD). The compn. can comprise a dry mixt., a dry inclusion complex or an aq. soln. The **salt**/**cyclodextrin** inclusion complex preferably provides an amt. of ziprasidone of at least 2.5 mgA/mL when the complex is dissolved in water at 40 % wt./vol. A variety of ziprasidone **salts** are preferred, including the mesylate, esylate, besylate, tartrate, napsylate, and tosylate. A soln. was prepd. contg. SBECD and ziprasidone mesylate.

L19 ANSWER 2 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2
AN 1997:801873 CAPLUS
DN 128:66485
TI Method of selecting a **salt** for making an inclusion complex
IN **Kim, Yesook**
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
PI EP 811386 A2 19971210
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
AI EP 97-302821 19970424
PRAI US 96-16866 19960507
DT Patent
LA English
AB Claimed are a method of locating one or more **salts** of a compd., the **salts** having a soly. in a **cyclodextrin** equal to or greater than a desired target soly., comprising obtaining a series of **salts** of the compd., measuring the equil. soly. of each **salt** in the series in the

cyclodextrin, and comparing each measured soly. with the target soly. Ziprasidone mesylate was dissolved in a 300 mg/mL .beta.-**cyclodextrin** sulfobutyl ether soln. to make a concn. of 27.3 mg/mL. The soln. was sterile filtered and filled into vials to give a product to be administered orally or by injections.

L19 ANSWER 3 OF 7 TOXLIT
AN 1998:22919 TOXLIT
DN CA-128-066485E
TI Method of selecting a **salt** for making an inclusion complex.
AU **Kim Y**
SO (1997). Eur. Pat. Appl. PATENT NO. 811386 12/10/1997 (Pfizer Inc.). CODEN: EPXXDW.
CY UNITED STATES
DT Patent
FS CA
LA English
OS CA 128:66485
EM 199804
AB Claimed are a method of locating one or more **salts** of a compd., the **salts** having a soly. in a **cyclodextrin** equal to or greater than a desired target soly., comprising obtaining a series of **salts** of the compd., measuring the equil. soly. of each **salt** in the series in the **cyclodextrin**, and comparing each measured soly. with the target soly. Ziprasidone mesylate was dissolved in a 300 mg/mL .beta.-**cyclodextrin** sulfobutyl ether soln. to make a concn. of 27.3 mg/mL. The soln. was sterile filtered and filled into vials to give a product to be administered orally or by injections.

L19 ANSWER 4 OF 7 TOXLIT
AN 1998:17180 TOXLIT
DN CA-128-039555W
TI Inclusion complexes of aryl heterocyclic **salts**.
AU Johnson KC; **Kim Y**; Shanker RM
SO (1997). PCT Int. Appl. PATENT NO. 9741896 11/13/1997 (Shanker, Ravi Mysore). CODEN: PIXXD2.
CY UNITED STATES
DT Patent
FS CA
LA English
OS CA 128:39555
EM 199804
AB Compns. comprise a pharmaceutically acceptable **salt** of an aryl heterocyclic compd., such as ziprasidone, in a **cyclodextrin**. Preferred **cyclodextrins** are .beta.-

cyclodextrin sulfbutyl ether (SBECD) and hydroxypropyl .beta.-**cyclodextrin** (HPBCD). The compn. can comprise a dry mixt., a dry inclusion complex or an aq. soln. The **salt/cyclodextrin** inclusion complex preferably provides an amt. of ziprasidone of at least 2.5 mgA/mL when the complex is dissolved in water at 40 % wt./vol. A variety of ziprasidone **salts** are preferred, including the mesylate, esylate, besylate, tartrate, napsylate, and tosylate. A soln. was prepd. contg. SBECD and ziprasidone mesylate.

L19 ANSWER 5 OF 7 USPATFULL
AN 95:25045 USPATFULL
TI Method for preparing enteric-coated oral drugs containing acid-unstable compounds
IN Min, Dong S., Seoul, Korea, Republic of
Um, Kee A., Suwon, Korea, Republic of
Kim, Yong S., Suwon, Korea, Republic of
Park, Pyong W., Seoul, Korea, Republic of
PA Sunkyong Industries Co., Ltd., Suwon, Korea, Republic of (non-U.S. corporation)
PI US 5399700 950321
AI US 92-997791 921229 (7)
PRAI KR 91-25847 911231
DT Utility
EXNAM Primary Examiner: Fan, Jane T.
LREP Kenyon & Kenyon
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 906
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method for preparing enteric-coated oral drugs containing acid-unstable compound, in particular an enteric-coated oral drug prepared in the form of acid-stable dosage units as inclusion complex formed by reacting benzimidazole derivative, acid-unstable compound, with **cyclodextrin** in alkaline solution.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L19 ANSWER 6 OF 7 SCISEARCH COPYRIGHT 1998 ISI (R)
AN 95:83443 SCISEARCH
GA The Genuine Article (R) Number: QB582
TI EXPERIMENTAL STUDIES IN METAL AFFINITY DISPLACEMENT CHROMATOGRAPHY OF PROTEINS
AU **KIM Y J**; CRAMER S M (Reprint)
CS RENSSELAER POLYTECH INST, HOWARD P ISERMANN DEPT CHEM ENGN, TROY, NY, 12180 (Reprint); RENSSELAER POLYTECH INST, HOWARD P ISERMANN DEPT CHEM ENGN, TROY, NY, 12180; ALBANY MED COLL, DEPT RES, ALBANY,

NY, 12208
CYA USA
SO JOURNAL OF CHROMATOGRAPHY A, (02 DEC 1994) Vol. 686, No. 2, pp. 193-203.
ISSN: 0021-9673.
DT Article; Journal
FS PHYS; LIFE
LA ENGLISH
REC Reference Count: 48
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Metal affinity displacement chromatography was employed for the purification of proteins. The mobile phase modifier imidazole was shown to exhibit complex induced gradients in these displacement systems resulting in different imidazole microenvironments in each protein displacement zone. Furthermore, the induced imidazole gradient produced an elevated displacer concentration at the rear of the displacement train. While adsorption isotherms measured under the initial carrier conditions were unable to predict these displacements, isotherms measured under the induced imidazole conditions qualitatively predicted the effluent displacement profiles. It is believed that these induced imidazole gradients speed up the kinetics of the displacement process and are in part responsible for the sharp boundaries seen in these separations. This work demonstrates the ability of this bioseparation technique to effect efficient multicomponent separations and illustrates the importance of mobile phase modifier effects in metal affinity displacement chromatography.

L19 ANSWER 7 OF 7 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 93-227279 [28] WPIDS
DNC C93-101238
TI Stabilisation of acid-unstable cpds., esp. drugs - by reaction with **cyclodextrin** in alkaline soln..
DC B02 B07
IN AN, U K; SOO, K Y; SUN, M D; UK, P P; **KIM, Y S**; MIN, D S; PARK, P U; UM, K A; AN, E G; HIEN, M D; **KIM, Y**; MIN, D; PARK, P; UM, K; PARK, P W
PA (GIEN-N) GIENG GONG EB CO LTD; (SUNK-N) SUNKYONG IND CO LTD
CYC 24
PI WO 9313138 A1 930708 (9328)* EN 40 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: BR CA HU JP RU
CN 1076124 A 930915 (9424)
TW 224049 A 940521 (9425)
EP 619825 A1 941019 (9440) EN
R: DE ES FR GB IT PT SE
US 5399700 A 950321 (9517) 17 pp
JP 07506088 W 950706 (9535) 11 pp
BR 9207000 A 951128 (9605)

CA 2127111 C 960521 (9632)
HU 70494 T 951030 (9732)
JP 2662518 B2 971015 (9746) 11 pp
EP 619825 B1 971029 (9748) EN 18 pp
R: DE ES FR GB IT PT SE
DE 69222950 E 971204 (9803)
ES 2111148 T3 980301 (9815)
RU 2105773 C1 980227 (9841)

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FDT EP 619825 A1 Based on WO 9313138; JP 07506088 W Based on WO 9313138; BR 9207000 A Based on WO 9313138; HU 70494 T Based on WO 9313138; JP 2662518 B2 Previous Publ. JP 07506088, Based on WO 9313138; EP 619825 B1 Based on WO 9313138; DE 69222950 E Based on EP 619825, Based on WO 9313138; ES 2111148 T3 Based on EP 619825

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AB WO 9313138 A UPAB: 950918

A method of stabilising an acid-unstable cpd. comprises reacting the cpd. with **cyclodextrin** in an alkaline soln., the ratio of the cpd. to the **cyclodextrin** being in the range of form 1:1 to 1:10.

USE - The method is used to stabilise drugs for use in enteric coated oral compsns., pref. benzimidazole cpds. of the formula (I) and their **salts** and esp. omeprazole.

In (I), R1 = H, OCH3, CF3 or tetrafluoroethoxy; R2 = H, NHCH3 or N(CH3)2; R3 = H, OCH3, aryloxy or propaziloxy (sic); R4 = H or CH3. The stabilised drugs have excellent storage stability, dissolution and absorption properties after oral admin.

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ABEQ US 5399700 A UPAB: 950508

Acid unstable omeprazole is stabilised by A) dissolving **cyclodextrin** in an aq. alkaline soln. at 40-70 deg.C and B) reacting omeprazole for 1-30 min with the **cyclodextrin** in the soln. to form an inclusion complex of omeprazole with **cyclodextrin**. The mol. ratio omeprazole:**cyclodextrin** is 1:1-10.

The alkali is pref. an alkaline hydroxide, esp. e.g. NaOH, Ba(OH)2, an alkaline **salt**, esp. e.g. Na borate, Na phosphate, Na citrate, an amine, esp. e.g. Et2NH, ethylene diamine,

dibutylamine, and/or a buffer, esp. e.g. a carbonate buffer.

USE/ADVANTAGE - Used for the prodn. of enteric coated oral drugs contg. acid unstable cpds. The drugs have excellent storage stability, dissolution and absorption properties after administration. A simple mfg. process.

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ABEQ EP 619825 B UPAB: 971209

A method for stabilising an acid-unstable compound comprising: reacting a benzimidazole derivative having the following structural formula (I) and pharmaceutically acceptable **salts** thereof as the acid-unstable compound with a **cyclodextrin** in an alkaline solution, the ratio of the acid-unstable compound to the **cyclodextrin** in the reaction being from 1 : 1 to 1 : 10. (I), wherein: R1 is selected from the group consisting of hydrogen, methoxy, trifluoromethyl and tetrafluoroethoxy radicals; R2 is selected from the group consisting of hydrogen, methylamine and dimethylamine radicals; R3 is selected from the group consisting of hydrogen, methoxy, aryloxy and propargyloxy radicals; and R4 is selected from the group consisting of hydrogen and methyl radicals, and wherein the alkaline solution consists essentially of an aqueous solution of an alkali selected from the group consisting of alkaline hydroxides, alkaline **salts**, amines, buffers and combinations thereof.

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